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Article type: Case series

## **Role of velscope in early detection of dysplasias with a light on its limitations – a case series**

Running title: Role of velscope in early detection of dysplasias

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### Abstract

Oral cancer accounts for 3% of global malignancies. In India, oral potentially malignant disorders are the first noticeable signs observed in the oral cavity, with a prevalence rate ranging from 13.2% to 13.9%. The absence of diagnosis, limited knowledge, and rising tobacco use contribute to the advancement of these precancerous lesions into oral carcinoma. The prevalence of mortality and morbidity related to oral cancer in India has risen, highlighting the need for readily available diagnostic tools. A novel method in this context is the visually-enhanced lesion scope (VEL scope), a compact and portable handheld instrument that enables direct visualisation of the oral cavity. VEL scope has been reported to be ideal adjunctive diagnostic tool for mass screening and determining the optimal biopsy site during surgical procedures.

A series of case reports is presented where VEL scope was employed as a supplementary diagnostic instrument to evaluate the precision of the device's diagnostic capabilities in various situations with a light on its limitations. A multidisciplinary approach is necessary to prevent the progression of Oral potentially malignant disorders like Oral submucous fibrosis, oral leukoplakia to malignancy. Autofluorescence-based imaging systems like VELscope have become increasingly popular in oral cancer screening due to their quick and noninvasive nature.

### Keywords

Dysplasias, oral leukoplakia, Velscope

### Introduction

Oral cancer is a type of malignancy that constitutes 3% of the total number of such malignancies worldwide.<sup>1,2</sup> Recent research has shown that oral potentially malignant illnesses are the first noticeable signs that might be observed in the oral cavity, with a prevalence rate ranging from 13.2% to 13.9%.<sup>3</sup> These disorders cause structural and functional changes in the oral mucosa, increasing the likelihood of developing oral squamous

cell carcinoma. The absence of diagnosis, limited knowledge, and the rising prevalence of tobacco use in India are significant contributing factors to the advancement of these precancerous lesions and diseases into oral carcinoma. Due to these contributing factors, a significant proportion of oral cancer cases in India are detected at stages III and IV.<sup>4</sup>

The prevalence of mortality and morbidity related to oral cancer in India has risen, highlighting the need for readily available diagnostic tools that are highly effective for the community. Several diagnostic methods are available for detecting dysplastic lesions in the oral cavity. These methods include traditional biopsy inspection, vital staining, and autofluorescence instruments. However, a novel method in this context was implementing an "Optical biopsy system" that uses the understanding of light in conjunction with tissue. The visually-enhanced lesion scope (VELscope) is a compact and portable handheld instrument that enables direct visualisation of the oral cavity. The VELscope has a high sensitivity rate of 96% and a specificity rate around 95%.<sup>5</sup> It works on the principle of autofluorescence. The nonharmful blue/violet light source (400–460 nm) highlights the oral tissues. The visualisation of these tissues is achieved by using long pass and notch optical filters, which selectively allow the passage of long wavelength green and red autofluorescence. When directly observed under fluorescent light, normal mucosa is pale green. This is considered fluorescence retention. Tissues that do not release the typical pale green autofluorescence and hence seem darker are classified as fluorescence loss. Due to the absence of direct contact with the patient, the risk of cross-contamination is reduced. This makes it an ideal diagnostic tool for mass screening and a useful adjunct for diagnosing suspicious lesions and determining the optimal biopsy site during surgical procedures.

In addition to detecting dysplastic alterations, VELscope can reveal underlying fungal, bacterial, and viral diseases, providing an extra benefit compared to traditional screening technologies.

## Case series

This study consists of a collection of case reports in which various disorders were evaluated utilizing VELscope inspection and subsequently corroborated using histopathological means to establish a definitive diagnosis. The VELscope was employed as a supplementary diagnostic instrument to evaluate the precision of the device's diagnostic capabilities in all the aforementioned situations.

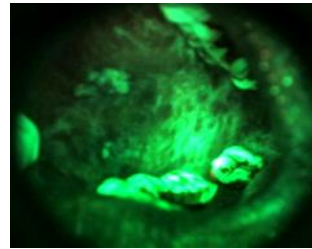
### Case report 1: Non homogenous Leukoplakia with Moderate Dysplasia

A middle-aged man of 47 years complained of a pain and tingling sensation in the mouth since one year. He had a 35-year history of tobacco smoking. Under white light examination, a red and white non homogenous lesion was detected on the right buccal mucosa.(Fig 1a) The lesion was non scrapable and provisionally a diagnosis of Non homogenous leukoplakia was given.Later the lesion was subjected to blue light with Velscope and there was loss of fluorescence noted at the lesion site and also surrounding the lesion.(Fig 1b). Analysis of the image indicates the presence of dysplasia, which justifies the need for an incisional biopsy. The provisional diagnosis was given as oral Leukoplakia, with other diagnoses that included Tobacco pouch keratosis and Candidiasis.. An incisional biopsy was conducted on the right buccal mucosa where the loss of fluorescence was noted. Under microscopic examination, thinning and abnormal growth of stratified squamous epithelium was observed that displayed characteristics of dysplasia, including excessive cell division in certain areas, darkened nuclei, changes in the ratio of nuclear to cytoplasmic material, and abnormal cell division extending to the middle third of the epithelium. An assortment of inflammatory cells, consisting mostly of neutrophils and lymphocytes, was observed in the underlying stroma. The presence of inflammatory cells and engorged blood vessels suggests an ongoing inflammatory process within the affected tissue.The extensive microscopic

observations are suggestive of moderate dysplasia. The patient was counselled regarding habit cessation and symptomatic treatment with antioxidant therapy was advised. Laser ablation was advised to prevent further progression and potential complications. Additionally, close monitoring and regular follow-up appointments are essential in order to assess the effectiveness of the treatment plan and ensure the patient's overall well-being.



1a



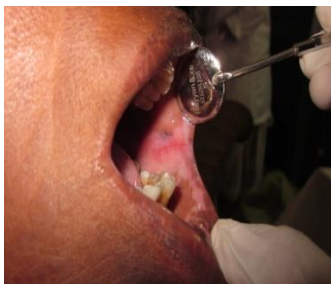
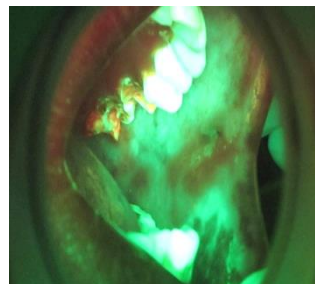
1b

**Fig 1a:** Non homogenous leukoplakia on right buccal mucosa under white light examination. **Fig 1b:** Loss of fluorescence shown as dark area at the lesion site on examination with Velscope.

### Case report 2: Oral Leukoplakia with Mild Dysplasia

A 65-year-old female reported with the complaint of a white patch on the inner lining of the left cheek with a prolonged habit of smoking pan and tobacco over 20 years. The patient reported no presence of ulceration, pigmentation, or growth in the afflicted area, and the remainder of the oral mucosa was unremarkable. The patient exhibited prominent dentition and had a habitual pattern of regular tobacco consumption. On clinical examination, a white lesion with reddish discoloration on it was detected on the left buccal mucosa. (Fig 2a) The provisional diagnosis was oral leukoplakia, and the possible differential diagnosis included lichenoid reaction and erythroplakia. The lesion was examined with Velscope (Fig 2b) and there was loss of fluorescence seen at the lesion site leading to the decision to do an incisional biopsy. Upon microscopic examination, squamous epithelium had

a consistent thickness and displayed characteristics suggesting mild dysplasia, including basal hyperplasia, lack of stratification, large rete ridges, cellular and nuclear pleomorphism, and reduced cell cohesion. In addition, there were notable veins with a sublayer that had spines, fibro cellular connective tissue with a moderate infiltration of inflammatory cells, mostly lymphocytes and plasma cells, many swollen capillaries, and a deeper layer consisting of adipose and skeletal muscle tissues. The overall diagnosis indicates the presence of mild dysplasia in the setting of leukoplakia. This inflammatory milieu, combined with the dysplastic changes, raises concerns about the development of malignant transformation. Management of this potentially pre-cancerous condition is imperative to prevent progression to malignancy. Therefore, a multidisciplinary approach involving close monitoring, targeted interventions, and patient education is warranted to ensure optimal outcomes for the patient.

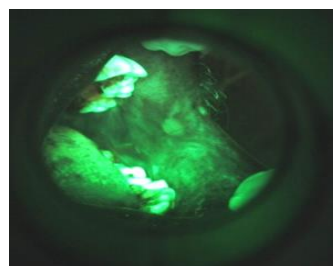
**2a****2b**

**Fig 2a.** Clinical picture of oral leukoplakia on the left buccal mucosa seen as white patch with red lesion on it. **Fig 2b.** Loss of fluorescence noted at the lesion site when examined with Velscope.

### **Case report 3: Oral leukoplakia with Mild Dysplasia**

A 52-year-old male presented with a white patch on the left buccal mucosa, indicating a potential oral health concern. The patient's overall health is reported good, with no notable pigmentation, growth, or specific symptoms, except for sharp teeth. He has been a smoker and alcohol consumer for the past 22 years. The lesion present for less than two weeks,

which prompts concern. Given the history and clinical presentation (Fig 3a), the provisional diagnosis leans towards Oral Leukoplakia. On velscopic examination, there was fluorescence loss adjacent to the white lesion. (Fig 3b) A biopsy is strongly advised to obtain a definitive diagnosis. The incisional biopsy revealed microscopic features indicative of Mild Dysplasia. The H&E stained soft tissue section exhibited ortho-keratotic stratified squamous epithelium with dysplastic characteristics, including basal cell hyperplasia, broad rete ridges, prominent nucleoli, and altered nuclear-cytoplasmic ratio in the lower third of the epithelium. The underlying fibrocellular connective tissue stroma displayed collagen fibre bundles, fibroblasts, moderate chronic inflammatory cell infiltration, and increased capillaries. Deeper stroma revealed skeletal muscle tissue, adipose tissue, and hemorrhagic areas suggesting potential invasion and disruption of surrounding tissues. These findings suggest a mild dysplastic process in the sampled tissue. The patient was counselled on habit cessation and put on antioxidant therapy. Surgical removal using laser was advised and follow up is crucial to observe the progression or regression of the lesion.

**3a****3b**

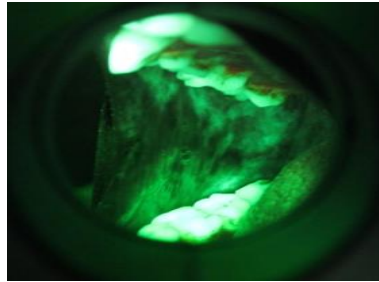
**Fig 3a:** Clinical image of leukoplakia on the left buccal mucosa **Fig 3b:** loss of fluorescence on the adjacent area to the white patch on Velscopic examination.

#### **Case Report 4 :Oral Frictional Hyperkeratosis on Buccal Mucosa**

A middle-aged man, aged 47 developed white patch on the right inner lining of his cheek which was evident since a month. The individual's general health is stated to be satisfactory, with no aberrant growth detected. The patient has a 12-year history of alcohol smoke consumption along with tobacco. There is no record of any symptoms associated with sharp teeth. Clinically, whitish patch with few grey areas were seen on the right buccal mucosa with the surface appeared to be rough (Fig 4a). A preliminary diagnosis of Frictional hyperkeratosis irt right buccal mucosa was given. On velscopic examination, few areas were bright due to strong keratin fluorescence and there was loss of fluorescence in few areas in proximity to the lesion site (Fig 4b). A full understanding of the underlying disease can be achieved with a biopsy. An incisional biopsy was conducted. The microscopic inspection showed a stratified squamous epithelium with a uniform thickness, a conspicuous granular layer, and wide, merged rete ridges. The connective tissue stroma beneath had a reticular pattern characterised by tightly packed collagen fibres, elongated fibroblasts, blood arteries with enlarged red blood cells, adipose tissue, neurovascular bundles, and bundles of skeletal muscle in the deeper stroma. The conclusive diagnosis suggests "Hyperkeratosis." The histopathology findings in this case report provide significant insights into the patient's condition. The presence of hyperkeratosis, as shown by the final diagnosis, implies an anomalous thickening of the outermost epidermal layer. This discovery aligns with the patient's clinical manifestation, since he had reported experiencing parched and coarse skin. The presence of a granular layer and merged rete ridges detected in the histological investigation provide additional evidence for diagnosing hyperkeratosis. The data suggest an elevated synthesis of keratinocytes and a disturbance in the regular process of skin cell replacement. Patient was educated regarding the cause and advised habit cessation as the frictional irritants are responsible for the keratosis in this case. Reevaluation after habit



cessation for every 2 weeks was suggested and if no signs of resolution are noted then surgical removal of the lesion is imperative.

**4a****4b**

**Fig 4a:** Frictional keratosis on right buccal mucosa **Fig 4b:** Bright and dark areas on the buccal mucosa on application of Velscope.

### Discussion

Oral cancer is a worldwide issue, and even with the availability of sophisticated treatments, there is a notable death rate caused by delayed discovery and diagnosis. From multiple clinical cases, it is evident that early diagnosis significantly enhances the prognosis. The VELscope, also called visually-enhanced lesion scope, functions as an auxiliary instrument to achieve this objective<sup>8</sup>. The autofluorescence-based imaging system is a crucial diagnostic tool that effectively detects lesions and improves the visibility of both premalignant and malignant lesions.

When directly observed under fluorescent light, normal mucosa is pale green. This is considered fluorescence retention. Tissues that do not release the typical pale green autofluorescence and hence seem darker are classified as fluorescence loss. To determine the difference, it is necessary to compare the suspicious abnormality with the surrounding tissue and the tissue on the other side of the body, which will serve as a reference for anatomical comparison.<sup>6,7</sup> When Loss of fluorescence is present, the VELscopic examination is

considered positive. This is because several changes occur, including: (i) the breaking of collagen cross-links, (ii) an increase in blood supply due to microvascularization and inflammation, and (iii) a decrease in flavine-adenine-dinucleotide and nicotinamide adenine dinucleotide (fluorochromes)<sup>9</sup>. The neoplastic development causes structural changes in the epithelium and the lamina propria, such as thickening of the epithelium, hyperchromatism, increased cellular pleomorphism, and increased microvasculature. These changes result in increased absorption or scattering of light, leading to altered autofluorescence. These alterations are observed in both inflammatory phenomena and dysplastic tissues<sup>10</sup>.

Optical methods, such as autofluorescence using VELscope-like devices, have become increasingly popular in oral cancer screening because they provide a quick and noninvasive alternative to biopsy. Therefore, it can serve as a screening tool for high-risk populations. The study conducted by Vibhute et al.,<sup>9</sup> determined that while the autofluorescence approach cannot replace a thorough oral examination, it can be utilised as a valuable supplementary diagnostic tool for monitoring high-risk patients. Koch et al. conducted a study that found VELscope to have a sensitivity of 97% and a specificity of 95.8% in diagnosing oral cancer.<sup>11</sup> Several research have examined the diagnostic efficacy of VELscope, including comparisons with conventional biopsies and investigations into its application in clinical settings. Poh et al.<sup>12</sup> showed that the VELscope can accurately identify the high-risk area surrounding the primary tumour, which is not visible during clinical examination prior to surgical removal. Tsui et al.<sup>13</sup>, conducted a comparison between the VELscope and toluidine blue in order to visualise the area surrounding a tumour. While toluidine blue selectively stained specific regions corresponding to early oral squamous cell carcinoma (OSCC), the VELscope detected a broader area corresponding to dysplasia.

In the first three case reports reported, Velscope played an important role in detecting early cases of dysplasia that are confirmed on histopathological examination. But then, in the

case of Hyperkeratosis, there was no evidence of dysplasia even after loss of fluorescence. Henceforth, it is imperative that Velscope can be used as an efficient adjunctive noninvasive tool in visualizing the mucosal abnormalities and not the only tool to diagnose dysplasias.

## **Conclusion**

In addition, the VELscope examination, which relies on the autofluorescence technique, is a straightforward, cost-effective, and noninvasive, user-friendly method. The gadget also has limitations as it does not aid in distinguishing between different types of lesions, such as premalignant, malignant, benign, or acute inflammation. It is an adjuvant technique in enhancing the abnormal lesions and cannot be the sole method of diagnosis. Nevertheless, it has been demonstrated to be an exceptional instrument for directing surgical processes. In conclusion, the highlighted cases demonstrated that VELscope can serve as a supplementary tool and enhance the effectiveness of the overall clinical evaluation.

The most reliable method for diagnosing malignancy is now through the process of performing a biopsy and subsequently examining the tissue sample under a microscope. However, as technology advances, the VELscope can be utilised by skilled professionals to enhance the effectiveness of the clinical examination.

These case studies demonstrate the utility of the VELscope in monitoring patients with a history of dysplasia and identifying the high-risk area surrounding the original lesion. These reports are also utilised to support the assertion that the VELscope has the ability to detect clinically hidden diseases.

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