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Evaluation of the diagnostic efficacy and spectrum of autofluorescence of benign, dysplastic and malignant lesions of the oral cavity using VELscope

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ABSTRACT

Objectives: Conventional oral examination and biopsy are the only reliable methods for the early detection of oral cancer at present. Autofluorescence examination of oral tissues using the VELscope has been suggested as an adjunctive tool for cancer detection and diagnosis. The aim of our study was to evaluate the efficacy of the VELscope in recognizing dysplastic and/or neoplastic changes in oral mucosal lesions that were identified on conventional oral examination.

Materials and methods: Two hundred patients with oral mucosal lesions were subjected to conventional oral examination followed by VELscope examination and their autofluorescence characteristics were compared with the histopathological diagnosis. The sensitivity, specificity, positive and negative predictive values of the VELscope examination was calculated.

Results: The VELscope examination showed sensitivity and specificity values of 76% (95% CI: 54.87–90.64%) and 66.29% (95% CI: 58.76–73.24%) respectively while the positive and negative predictive values were 24.36% (95% CI: 19.22–30.36%) and 95.08% (95% CI: 90.52–97.51%) respectively.

Conclusion: The VELscope examination alone cannot provide a definitive diagnosis as to the presence of dysplastic tissue change. In spite of having a reasonable sensitivity, the high number of false-positive results limits its efficiency as an adjunct. However, a high negative predictive value can serve to alleviate patient anxiety regarding suspicious mucosal lesions in a general practice setting.

Introduction

In individuals exposed to risk factors; the prevention and early detection of oral cancer play a significant role in increasing the survival rates [1,2]. In the absence of a definitive approach, screening of oral cancer is still largely based on conventional oral examination (COE) and scalpel biopsy in case of suspicious lesions [3,4]. Since visible changes in the oral mucosa are known to precede the development of virtually all oral squamous cell carcinomas (OSCCs), various adjunctive techniques have been introduced with the aim to assist in the detection of early cancerous mucosal changes that can be occult to visual inspection [5,6].

The use of autofluorescence as a diagnostic tool for cancer detection was for the first time described as early as in 1924 [7]. It is based on the principle that the naturally occurring fluorochromes that are located in the epithelium (eg.nicotinamide adenine dinucleotide or NADH and flavin adenine dinucleotide or FAD) and the submucosa (e.g. collagen and elastin) when irradiated between the wavelengths 375 and 440 nm, show fluorescence in the green spectral range [5,8].

The VELscope (LED Medical Diagnostics Inc., Burnaby Canada) utilises the same principle to enhance oral mucosal abnormalities by direct tissue autofluorescence [9–11]. At the excitation wavelengths (375–440 nm), normal, unaltered mucosa emits a pale green autofluorescence when viewed through a filter. However; dysplastic tissues lose fluorescence emission power due to a disruption in the distribution of the fluorochromes and appear darker in colour in comparison to the surrounding healthy tissue [5].

Neoplastic tissues are thus expected to cause fluorescence visualisation loss (FVL) and appear as a dark area. Several studies have investigated the effectiveness of the VELscope in detecting malignant changes in the oral mucosa and have reported sensitivity and specificity values ranging from 22% to 100% and 12% to 100% respectively (Table 1) [12–26]. However, a majority of these studies were conducted on patients with oral potentially malignant disorders (OPMDs)

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Table 1
Clinical trials evaluating the efficacy of VELscope in detecting oral cancer and oral potentially malignant disorders.

Author	Year	Study design	Sample size	Selection criteria	Sensitivity	Specificity
Sharwani A et al. [13]	2006	Cross-sectional study	79	Clinically suspicious oral leukoplakia	83–90%	79–89%
Lane et al. [14]	2006	Cross-sectional study	44	Oral leukoplakia patients	98%	100%
Mehrotra et al. [15]	2010	Cross-sectional study	156	Oral mucosal white lesions	50%	38.9%
Awan KH et al. [12]	2011	Prospective study	126	Patients with OPMD	84.1%	15.3%
Koch et al. [17]	2011	Prospective blinded clinical trial	78	Oral squamous cell carcinoma (OSCC) or suspicious epithelial lesion	93%	16%
Pardeni et al. [19]	2011	Cross-sectional study	175	Patients with at least one clinical oral lesion	OSCC: 96.4% Dysplasia:71%	NA
Scheer et al. [21]	2011	Prospective study	64	Patients at risk of OSCC and prior history of OSCC	100%	80.8%
Babiuch et al. [24]	2012	Pilot study	50	Patients with OSCC and lip cancer	100%	12.5%
Farah CS et al. [22]	2012	Prospective study	112	Patients with potentially malignant oral mucosal lesion	30%	63%
Marzouki et al. [20]	2012	Prospective single blind study	85	History of smoking, alcohol use or previous head and neck cancer	92%	77%
Mc Namara K et al. [23]	2012	Cross sectional study	130	Consecutive recruitment for routine dental care	NA	NA
Rana et al.[18]	2012	Cross sectional study	123	Patients with OPMD	100%	74%
Hanken H et al.[16]	2013	Single blinded study	120	Patients with OPMDs	22%	8.4%
Sawan et al.[25]	2015	Prospective study	748	Consecutive recruitment for routine dental care	74.1%	96.3%
Salas et al.[26]	2015	Pilot study	30	Patients with mucosal pathology	40%	80%
Present study	2017	Prospective study	200	Patients with mucosal pathology	76%	66.29%

[12–16,18,22] or a prior history of OSCC [17,20,21,24].

The aim of the present study was to evaluate the efficacy of the VELscope in detecting dysplastic and/or neoplastic changes in all the oral mucosal lesions that were detected on COE. We also intended to obtain data on the autofluorescence pattern of a variety of benign, dysplastic and neoplastic oral mucosal lesions in order to evaluate the autofluorescence characteristics of these lesions irrespective of their biologic behaviour.

Materials and methods

Patients with oral mucosal lesions reporting to the Department of Oral Pathology and Microbiology, over a period of 10 months (November 2015 to August 2016) were included in the present study. Participation in the study was voluntary and followed informed consent. The study was approved by the Institutional Ethics Committee (EC-67/OPATH-07ND/2017). It was designed according to the principles manifested in the Declaration of Helsinki and was consistent with the guidelines of Good Clinical Practice given by the International Conference on Harmonization (ICH-GCP) [27].

Conventional oral examination of 200 patients with oral mucosal lesions was performed under incandescent operatory light and a provisional clinical diagnosis was recorded. This was followed by autofluorescence examination using the VELscope (LED Medical Diagnostics Inc, Burnaby, Canada). A photo documentation of all the lesions during COE, as well as the VELscope examination, was carried out for future review and correlation.

Depending on their autofluorescence characteristics as determined by the manufacturer's literature, the lesions were divided into two groups. Group 1 included lesions that exhibited a loss of autofluorescence (fluorescence visualisation loss or FVL) and appeared dark compared to the surrounding unaltered tissue with pale green autofluorescence thus, indicating malignant or dysplastic change. Group 2 included lesions that exhibited retention of autofluorescence (fluorescence visualisation retained or FVR) and showed no change in autofluorescence when compared to the surrounding unaltered tissue [12].

Only a complete FVL was rated as malignant or dysplastic [21] and lesions that demonstrated autofluorescence patterns other than a complete FVL were included in the FVR group.

The lesions were biopsied for histopathological assessment after obtaining appropriate informed consent. Hematoxylin and eosin staining of the formalin fixed paraffin embedded tissue sections was carried out and assessed by two experienced oral pathologists who were blinded to the VELscope findings and were not involved with the clinical arm of the study.

The results of the VELscope examination results were compared with the histopathological diagnosis. A true-positive result was considered when a lesion demonstrating FVL was confirmed to be malignant or dysplastic following histopathologic assessment, while a false-positive result was considered when a lesion demonstrating FVL turned out to be benign on histopathological examination. A true-negative result was considered when FVR was noted in a lesion that was confirmed to be benign on histopathologic examination and a false-negative result was considered when a lesion demonstrating FVR was confirmed to be malignant on histopathological assessment.

The sensitivity score measured the proportion of malignant and dysplastic lesions that were correctly identified with the VELscope while the specificity score measured the proportion of benign lesions that were correctly identified with the VELscope. The positive predictive value (PPV) indicated the proportion of lesions with positive VELscope results that were correctly diagnosed as malignant on histopathological assessment whereas, the negative predictive value (NPV) indicated the proportion of lesions with negative VELscope results that were correctly diagnosed as benign on histopathological assessment. The sensitivity, specificity, positive and negative predictive values were evaluated from a contingency table (Table 2) [28,29].

Results

The VELscope examination of 200 oral mucosal lesions revealed that 78 (39%) lesions belonged to Group 1 while the remaining 122 (61%) lesions belonged to Group 2 (Fig. 1).

In addition to FVL and FVR, some of the lesions examined in our study exhibited autofluorescence patterns that included fluorescence

Table 2
Contingency table for calculating the sensitivity, specificity, positive and negative predictive values of the VELscope examination.

Study group	VELscope findings	Histopathological assessment		
		Malignant	Benign	
Group 1	FVL	TP	FP	PPV TP/(TP + FP)
Group 2	FVR	FN	TN	NPV TN/(FN + TN)
		Sensitivity TP/(TP + FN)	Specificity TN/(FP + TN)	

FVL, fluorescence visualisation loss; *FVR*, fluorescence visualisation retained; *TP*, true positive; *FP*, false positive; *FN*, false positive; *TN*, true negative; *PPV*, positive predictive value; *NPV*, negative predictive value.

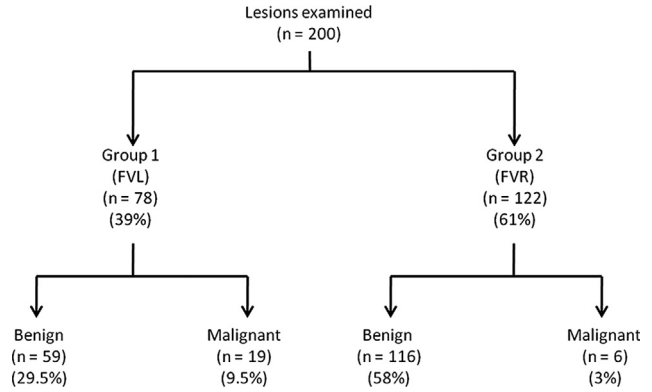

Fig. 1. Tissue autofluorescence characteristics of all lesions (n = 200). Lesions showing FVL* were included in Group 1 while those showing FVR* were included in Group 2.

Table 3
Autofluorescence characteristics of the lesions examined using the VELscope *FVL,* fluorescence visualisation loss*; FVR,* fluorescence visualisation retained*; FVI,* fluorescence visualisation increased.

Sr. no	Clinical diagnosis	Total (n)	Autofluorecence characteristics				
			FVL	FVR	FVL + FVR	FVI	FVI + FVL
1	Oral submucous fibrosis	58			58		
2	Leukoplakia	43	03	02		38	
3	Oral squamous cell carcinoma	23	17	01	01	04	
4	Oral lichen planus	22	18	04			
5	Pyogenic granuloma	21	19	02			
6	Fibroma	08	07		01		
7	Mucocele	07		07			
8	Inflammatory hyperplasia	05	05				
9	Verrucous hyperplasia	03		02		01	
10	Lichenoid reaction	02	02				
11	Lipoma	02	02				
12	Pemphigus	02	02				
13	Verrucous carcinoma	01	01				
14	Salivary gland neoplasm	01	01				
15	Central giant cell lesion	01	01				
16	Osteonecrosis	01					01
Total (n)		**200**	**78**	**18**	**60**	**43**	**01**

visualisation increase or FVI (lesional area exhibiting increased autofluorescence compared to the surrounding tissue) and a combination of FVL and FVR (lesional area exhibiting patches of FVL as well as FVR) or FVI and FVR (lesional area exhibiting patches of FVI as well as FVR) (Table 3). Owing to the lack of specific criteria to characterise these lesions based on their autofluorescence patterns, they were included in the FVR group for statistical analysis.

On histopathological assessment, 175 (87.5%) of the 200 lesions examined were benign and the remaining 25 (12.5%) were malignant. Of these, 59 (29.5%) benign and 19 (9.5%) malignant lesions belonged to Group 1 (Fig. 2A-2F) whereas, 122 (61%) benign and 6 (3%) malignant lesions belonged to Group 2 (Table 4). On comparison of the VELscope results with the histopathological diagnosis, the number of lesions with true-positive, false-positive, true-negative and false-negative values were found to be, 19 (9.5%), 59 (29.5%), 116 (58%) and 6 (3%) respectively while, the sensitivity, specificity, positive and negative predictive values were, 76% (95% CI: 54.87–90.64%), 66.29% (95% CI: 58.76–73.24%), 24.36% (95% CI: 19.22–30.36%) and 95.08% (95% CI: 90.52–97.51%) respectively (Table 5).

For descriptive purposes, Group 2 lesions were further divided into four subgroups based on their autofluorescence characteristics as; Group 2A (lesions showing FVR) (Fig. 3), Group 2B (lesions showing a combination of FVL and FVR) (Fig. 4), Group 2C (lesions showing FVI) (Fig. 5) and Group 2D (lesions showing a combination of FVI and FVL) (Fig. 6) with 18, 60, 43 and 1 lesions each.

Group 2A included 17 (8.5%) benign and 1 (0.5%) malignant lesion, Group 2B included 59 (29.5%) benign and 1 (0.5%) malignant lesion, Group 2C included 39 (19.5%) benign and 4 (2%) malignant lesions whereas, the only lesion included in Group 2D was found to be benign on histopathological assessment (Table 6).

Discussion

The present study analysed oral mucosal lesions in 200 patients using COE followed by VELscope examination. The autofluorescence characteristics of these lesions were then compared with the histopathological diagnosis.

The statistical analysis revealed the sensitivity and specificity values of the VELscope examination to be 76% (95% CI: 54.87–90.64%) and 66.29% (95% CI: 58.76–73.24%) respectively while the positive and negative predictive values were 24.36% (95% CI: 19.22–30.36%) and 95.08% (95% CI: 90.52–97.51%) respectively. The high negative predictive value was justified due to the high rate of false-positive results and a low specificity whereas; the false-negative results limited the sensitivity of the VELscope examination.

Meticulous visual inspection of suspicious lesions under white light and a scalpel biopsy followed by a period of “watchful waiting” of 3 months duration for rest of life seems to be the only reliable approach currently available for ruling out or detecting oral cancer at an early stage [16].

Tissue autofluorescence is said to represent the metabolic and biochemical status of the cells by relying on the fluorescent emission produced by the endogenous fluorophores in response to exposure to light of a specific wavelength. Malignant lesions are expected to demonstrate an altered autofluorescence profile than normal oral mucosa as a result of alterations in these endogenous fluorophores [8,30–32].

The alterations include a breakdown of the collagen cross-links in the connective tissue and a reduction in flavin adenine dinucleotide (FAD) and nicotinamide adenine dinucleotide (NAD) in the epithelium. In addition, physical factors that affect light absorption such as increased blood absorption due to micro-vascularization and inflammation, epithelial thickening, and nuclear back-scattering result in malignancies demonstrating lower autofluorescence intensities than normal oral mucosa [33,34].

The present study also aimed to obtain autofluorescence data on a variety of histologically distinct lesions so as to ascertain the ability of the VELscope to discriminate between lesions with similar autofluorescence patterns. In Group 1, FVL was found to be a feature of malignant as well as benign lesions (Fig. 2A–F). While FVL is an expected finding in malignant lesions, its occurrence in benign inflammatory lesions like pyogenic granuloma, fibro-epithelial hyperplasia, and central giant cell lesion can lead to false-positive results as seen in our study. The FVL seen in these cases has been attributed to the increased sub-epithelial blood flow and altered metabolic activity of the inflamed mucosa [8]. Thus, benign inflammatory lesions in addition to mimicking a malignancy clinically may also demonstrate similar autofluorescence characteristics resulting in an overdiagnosis of malignancy.

Early dysplastic changes usually precede the development of invasive OSCC [1,7,35].These are expected to cause an alteration in the endogenous fluorochromes and manifest as FVL. However, on the contrary, our study included 1 case of severe epithelial dysplasia demonstrating FVR (Fig. 3D–F), 1 case of oral squamous cell carcinoma

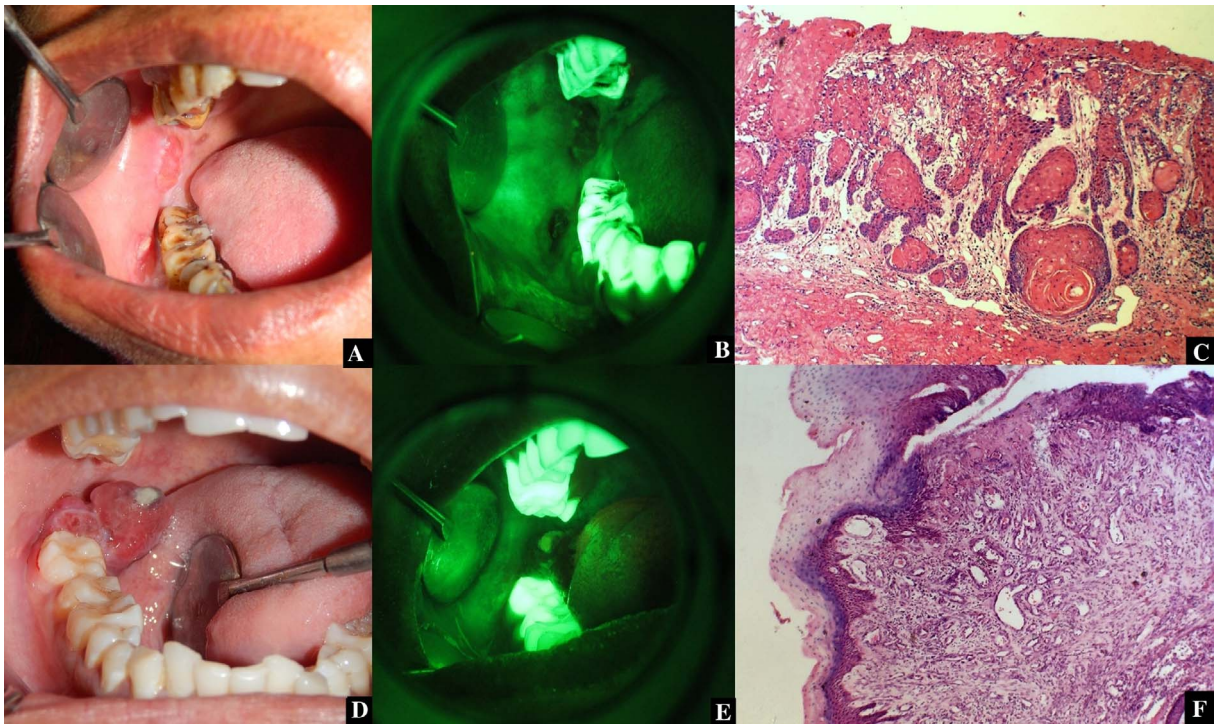

Fig. 2. (A) Conventional oral examination showing an erythematous ulcerative lesion in the right buccal mucosa and vestibule; (B) VELscope examination showing FVL; (C) lesion diagnosed histopathologically as oral squamous cell carcinoma (true-positive); (D) Conventional oral examination showing a proliferative, erythematous soft tissue growth in the right retromolar area; (E) VELscope examination showing FVL; (F) lesion diagnosed histopathologically as pyogenic granuloma (true-negative).

(OSCC) demonstrating a combination of FVL and FVR in the same lesion and 4 cases of OSCC demonstrating FVI (Fig. 5). Consequently, these lesions gave rise to false-negative results thus affecting the sensitivity of the device. These findings suggest that the VELscope is unable to accurately differentiate between dysplastic and non-dysplastic lesions and are in agreement with Babuich et al. [24] who stated that autofluorescence was not highly specific for dysplasias and cancers.

The present study included 58 cases of oral submucous fibrosis (OSF) exhibiting dual autofluorescence with the affected mucosa exhibiting focal areas of FVL interspersed between areas of FVR (Fig. 4). Presently, no clear criteria exist to classify the lesions that exhibit a combination of FVL and FVR in the same lesion. Ours is probably the first study to report the combined autofluorescence pattern in OSF. This dual autofluorescence in OSF could be attributed to the overlap in the wavelengths of healthy oral mucosa (between 375 and 440 nm) [21] and fibrosis (between 380 and 460 nm) [36] which may be responsible for the areas of FVR. Areca nut and its metabolites are known to cause physical and chemical irritation leading to microtrauma and inflammation of the underlying mucosa [37,38]. The altered metabolic activity of the inflamed mucosa may be responsible for the focal areas of FVL seen in OSF. OSF has a malignant transformation rate of 7–13% [39]. Owing to their inconclusive autofluorescence characteristics,

Table 4
Comparison of the VELscope findings with histopathology.

Group	No. of lesions	Histopathological diagnosis			
		Malignant	No. of Lesions	Benign	No. of Lesions
1 (FVL)	78 (39%)	Oral squamous cell carcinoma	17 (21.79%)	Pyogenic granuloma	19 (24.35%)
		Mucoepidermoid carcinoma	01 (1.28%)	Oral lichen planus	18 (23.07%)
		Verrucous carcinoma	01 (1.28%)	Fibro-epithelial hyperplasia	07 (8.97%)
				Inflammatory hyperplasia	05 (6.41%)
				Leukoplakia	03 (3.84%)
				Lichenoid reaction	02 (2.56%)
				Lipoma	02 (2.56%)
				Pemphigus	02 (2.56%)
				Central giant cell lesion	01 (1.28%)
		Total	**19 (9.5%)**	**59 (29.5%)**	
2(FVR)	122(61%)	Oral squamous cell carcinoma	04 (3.28%)	Oral submucous fibrosis	58 (47.54%)
		Severe epithelial dysplasia	01 (0.82%)	Leukoplakia	40 (32.78%)
		Oral squamous cell carcinoma	01 (0.82%)	Mucocele	07 (5.73%)
				Oral lichen planus	04 (3.27%)
				Verrucous hyperplasia	03 (2.45%)
				Pyogenic granuloma	02 (2.56%)
				Osteonecrosis	01 (0.82%)
				Tubulo-papillary adenoma	01 (0.82%)
		Total	**06 (3%)**	**116 (58%)**	
Total	**200 (100%)**	**25 (12.5%)**		**175 (87.5%)**	

Table 5
Sensitivity, specificity, positive and negative predictive values of the VELscope examination with 95% confidence interval.

Study group	VELscope findings	Histopathological assessment		Statistic % (95% C.I)
		Malignant	Benign	
Group 1	FVL (n = 78)	TP (n = 19)	FP (n = 59)	PPV 24.36% (19.22–30.63%)
Group 2	FVR (n = 122)	FN (n = 6)	TN (n = 116)	NPV 95.08% (90.52–97.51%)
Statistic % (95% C.I)		Sensitivity 76% (54.87–90.64%)	Specificity 66.29% (58.76–73.24%)	

FVL, fluorescence visualisation loss; *FVR*, fluorescence visualisation retained; *TP*, true positive; *FP*, false positive; *FN*, false positive; *TN*, true negative; PPV, positive predictive value; NPV, negative predictive value.

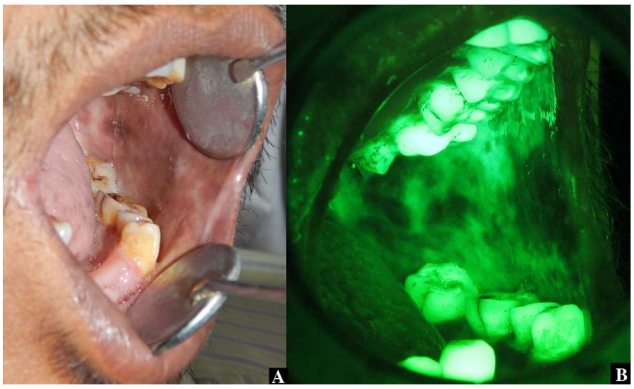

Fig. 4. (A) Conventional oral examination showing blanched and fibrotic buccal mucosa in a patient with oral submucous fibrosis; (B) VELscope examination showing a combination of FVL and FVR in the same lesion.

cases of OSF carry the risk of incorrect interpretation and put the onus on the clinical judgement of the practitioner thereby, undermining the efficacy of the VELscope as an adjunct to COE.

An increase in keratinisation is a feature common to some benign as well as malignant lesions. Keratin is known to demonstrate an increase in autofluorescence with a decrease in wavelength [40]. As a result, such lesions would be expected to demonstrate FVI compared to normal mucosa upon excitation using the VELscope. Consequently, in our study, FVI was found to be a feature of leukoplakia as well as OSCC (Fig. 5). The FVL criteria for suspecting malignant conversion could not be applied to these lesions leading to false-negative results thus suggesting that, lesions exhibiting FVI limit the ability of the VELscope to detect malignant change.

Group 2D in our study included a single case of suspected osteonecrosis of the jaw, with the exposed bone exhibiting FVI and the surrounding mucosa exhibiting FVL (Fig. 6). Bone fluorescence is dependent on calcification [41] and viable bone is known to show a bright greenish autofluorescence, while necrotic bone areas show no or only very pale autofluorescence. This principle has been used to delineate healthy bone from unhealthy bone during the surgical therapy of bisphosphonate-related osteonecrosis of the jaw (BRONJ) [42]. However, no criteria exist for the interpretation of bone fluorescence with respect to dysplastic and/or malignant changes.

Overall, the results of our study suggest that FVL is in itself a poor indicator of the nature of oral mucosal lesions and that neither FVL nor FVR is exclusive to either malignant or benign lesions. Our study also showed that the VELscope examination has a high negative predictive value of 95.08% (95% CI: 90.52–97.51%). These findings suggest that the ability of the VELscope to rule out rather than to indicate the presence of malignant change may contribute more to its effectiveness as an adjunct in a general practice setting. This may prove to be useful especially to alleviate both patient and practitioner concerns regarding a clinically suspicious oral mucosal lesion. It may also serve as a tool to augment patient compliance for a biopsy procedure. Using the VELscope examination as an intermediate between COE and a biopsy may lead to a reduced reluctance in the patient to undergo the biopsy procedure when compared to the patient being suggested a biopsy directly following COE. However, further studies are needed to confirm the effect of the VELscope examination on patient compliance.

Comparing our results with literature, Hanken et al. [16] examined

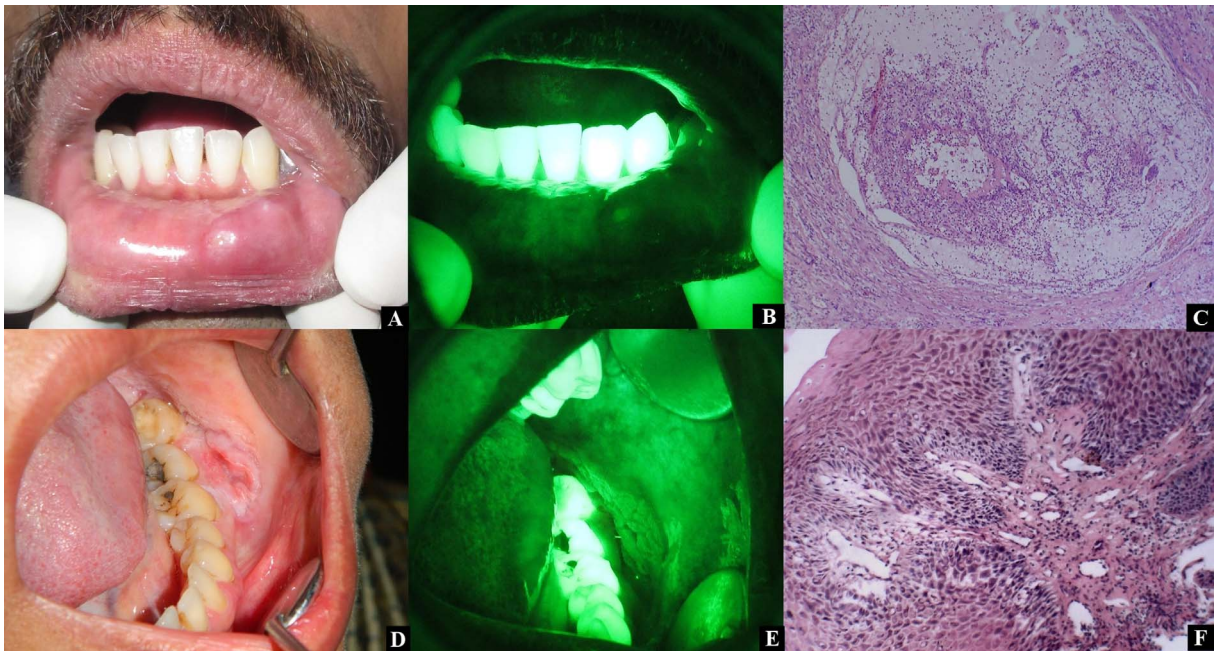

Fig. 3. (A) Conventional oral examination showing a well-defined, dome-shaped swelling on the left side of the lower lip; (B) VELscope examination showing FVR; (C) lesion diagnosed histopathologically as mucous extravasation cyst (true-negative); (D) Conventional oral examination showing an ulcerative lesion in the left buccal vestibule; (E) VELscope examination showing FVR; (F) lesion diagnosed histopathologically as severe epithelial dysplasia (false-negative).

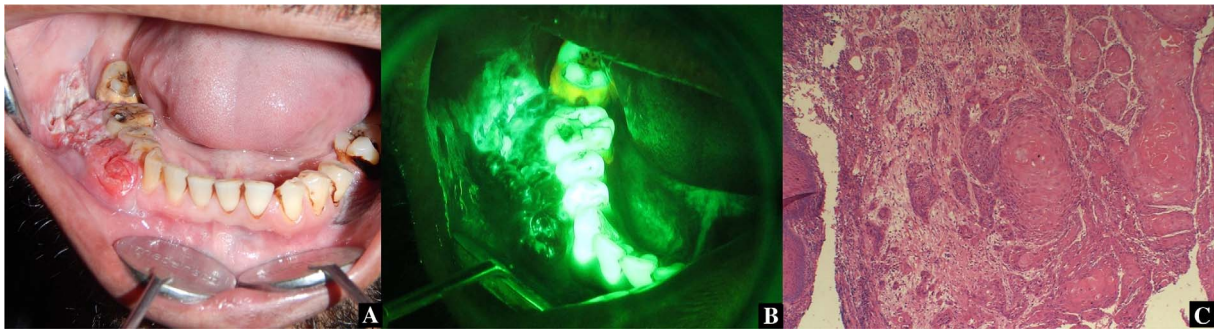

Fig. 5. (A) Conventional oral examination showing an extensive ulcero-proliferative growth with keratinised surface in the right buccal vestibule and alveolar ridge; (B) VELscope examination showing FVI*; (C) lesion diagnosed histopathologically as oral squamous cell carcinoma (false-negative). **FVI,* fluorescence visualisation increased.

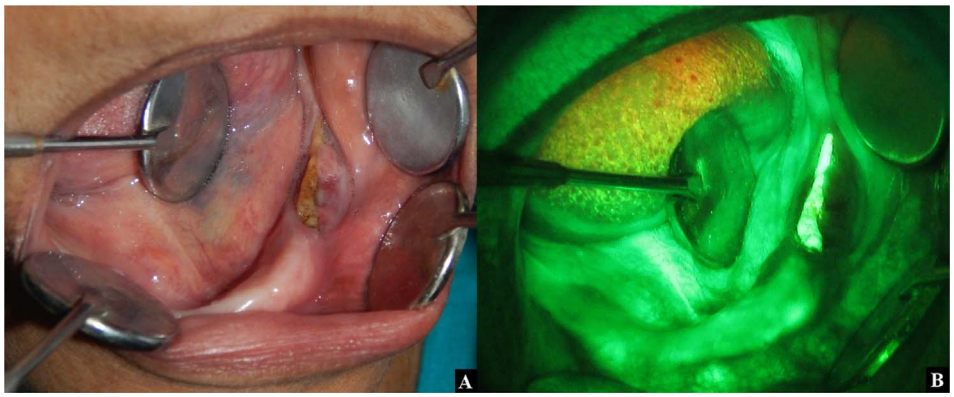

Fig. 6. (A) Conventional oral examination showing an area of exposed bone surrounded by an erythematous area on the left alveolar ridge in a suspected case of osteonecrosis; (B) VELscope examination showing a combination of FVI and FVL.

Table 6
Comparison of autofluorescence characteristics of the grouped lesions with histopathology.

Group	No. of lesions	Histopathological Diagnosis			
		Malignant	No. of lesions	Benign	No. of lesions
1 (FVL)	78 (39%)	Oral squamous cell carcinoma	17 (21.79%)	Pyogenic granuloma	19 (24.35%)
		Mucoepidermoid carcinoma	01 (1.28%)	Oral lichen planus	18 (23.07%)
		Verrucous carcinoma	01 (1.28%)	Fibro-epithelial hyperplasia	07 (8.97%)
				Inflammatory hyperplasia	05 (6.41%)
				Leukoplakia	03 (3.84%)
				Lichenoid reaction	02 (2.56%)
				Lipoma	02 (2.56%)
				Pemphigus	02 (2.56%)
				Central giant cell lesion	01(1.28%)
2A (FVR)	18 (9%)	Severe epithelial dysplasia	01 (5.55%)	Mucocele	07 (38.88%)
				Oral lichen planus	04 (22.22%)
				Verrucous hyperplasia	02 (11.11%)
				Leukoplakia	02 (11.11%)
				Pyogenic granuloma	02 (11.11%)
2B (FVL + FVR)	60 (30%)	Oral squamous cell carcinoma	01 (1.67%)	Oral submucous fibrosis	58 (96.66%)
				Tubulo-papillary adenoma	01 (1.67%)
2C (FVI)	43 (21.5%)	Oral squamous cell carcinoma	04 (9.31%)	Leukoplakia	38 (88.37%)
				Verrucous hyperplasia	01 (2.32%)
2D (FVI + FVL)	01 (0.5%)			Osteonecrosis	01 (100%)
Total	**200 (100%)**		**25 (12.5%)**		**175 (87.5%)**

120 patients with suspicious oral lesions and reported the sensitivity and specificity values of the VELscope examination to be 22% and 8.4% respectively. They stated that the VELscope was more promising than COE in detecting precursor oral malignant lesions. Koch et al. [17] reported a higher sensitivity (97%) and specificity of (95.8%) of the VELscope in diagnosing OSCC. Rana et al. [18] in their study compared VELscope examination with COE and reported that using the VELscope leads to higher sensitivity (100% vs. 17%), but a lower specificity (74% vs. 97%). In another study, McNamara et al. [23] concluded that COE is more valid than a VELscope examination in routine screening for OPMDs and stated that careful, systematic visual and tactile examination of the entire oral cavity on a regular basis remains the gold standard for early detection of OPMD. To the best of our knowledge, no prospective trial has confirmed that the VELscope was successful in identifying occult lesions that were not diagnosed by conventional oral examination and palpation alone.

A drawback of our study was that it included very few cases of OPMDs and OSCC due to the reluctance of some patients to undergo a biopsy procedure. As a result, the true prevalence could not be calculated in these cases. Hence, the PPV and NPV values should be interpreted with caution keeping in mind that they are a function of the sample prevalence. Although previous studies have evaluated autofluorescence largely in OPMDs and OSCC, the present study differs by including benign lesions, some of which in addition to clinically mimicking malignancy also exhibited FVL on VELscope examination. This population can be considered to be representative of the patient mix in a general dental practice.

We also suggest that further prospective trials with adequate follow-up and histopathological confirmation have to be conducted in a primary care setting to evaluate the efficacy of the VELscope as a screening tool in oral cancer and pre-cancer detection.

Further, adequate skill and training are required while interpreting the VELscope findings and the examination itself is highly subjective. Scheer et al. [21] suggested using quantification of fluorescence loss, for example; expressed as a ratio to surrounding normal tissue or analysis of the emitted spectrum of light, to assist in the characterisation of the lesions. Recently, Huang et al. [43] developed a novel data analysis algorithm to quantify the VELscope findings based on the intensity and heterogeneity in combination with a quadratic discriminant analysis (QDA) binary classifier to discriminate between oral lesions and normal oral mucosa. The authors suggest that since tissue autofluorescence images can be detected by using different light source bands, future development of multiple bands of light sources for detecting different tissue autofluorescence might contribute to being able to differentiate between precancerous oral lesions and oral cancer. We support their opinion and feel that characterising the fluorescence spectrum of oral mucosal lesions based on their biological behaviour and wavelength specificity may prove to be helpful in improving the efficacy of this device.

The interpretation of the VELscope results is further compounded by the lack of specific criteria to characterise lesions based on their autofluorescence patterns. Until these issues are addressed, this device may find little support as an effective cancer screening adjunct in the hands of an inexperienced operator. A thorough and systematic COE with white light, careful digital palpation, and scalpel biopsy followed by histopathological assessment remain the gold standard for the examination and evaluation of any suspicious oral mucosal lesion [44,45].

Conclusion

Due to the low specificity of the autofluorescence examination for discriminating dysplasias and cancers from benign lesions, the VELscope cannot provide a definitive diagnosis as to the presence of dysplastic tissue change. Its use requires a significant understanding of mucosal pathology, and the interpretation of results requires skill and training. Additionally, the false-positive results limit its efficiency. However, a high negative predictive value indicates that the VELscope is better equipped to rule out the presence of malignant change and can serve to alleviate patient and practitioner concerns regarding a clinically suspicious oral mucosal lesion. Even so, the VELscope examination alone cannot fully replace conventional oral examination, surgical biopsy and histopathological evaluation, which still represent the gold standard for a definitive diagnosis.

Conflict of interest

None declared.

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