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INFLUENCE OF FLUORESCENCE ON SCREENING DECISIONS FOR ORAL MUCOSAL LESIONS IN COMMUNITY DENTAL PRACTICES

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Abstract

Quality of oral screening examinations is dependent upon the experience of the clinician and can vary widely. Deciding when a patient needs to be referred is a critical and difficult decision for general practice clinicians. A device to aid in this decision would be beneficial.

Objectives—To examine the utility of direct fluorescence visualization (FV) by dental practitioners as an aid in decision-making during screening for cancer and other oral lesions.

Methods—Dentists were trained to use a stepwise protocol for evaluation of the oral mucosa: medical history, head, neck and oral exam and fluorescent visualization exam. They were asked to use clinical features to categorize lesions as low (LR), intermediate (IR) or high (HR) risk and then to determine FV status of these lesions. Clinicians made the decision of which lesions to reassess in 3 weeks and based on this reassessment, to refer forward.

Results—Of 2404 patients screened over 11 months, 357 initially had lesions with 325 (15%) identified as LR, 16 (4.5%) IR and 16 (4.5%) HR. Lesions assessed initially as IR and HR had a 2.7 fold increased risk of FV loss persisting to the reassessment appointment versus the LR lesions. The most predictive model for lesion persistence included both FV status and lesion risk assessment.

Conclusion—A protocol for screening (assess risk, reassess and refer) is recommended for the screening of abnormal intraoral lesions. Integrating FV into a process of assessing and reassessing lesions significantly improved this model.

Keywords

Oral cancer screening; precancerous conditions/diagnosis; mouth neoplasms/prevention & control; early detection of cancer/methods; awareness; health professionals/education; referral and consultation; fluorescence visualization

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Conflicts of Interest

The project received 10 VELScope units as a donation from LED Dental Inc., Burnaby, British Columbia, Canada.

Introduction

The advent of adjunct tools for use as part of the conventional oral examination has been a driving force for change in the screening activity in community practices. Such devices presently include toluidine blue, brush cytology, reflectance visualization and, more recently, autofluorescence imaging. However, validation of these tools has been mainly restricted to high-risk referral clinic settings with use by experienced personnel, with little work done in community settings.

In this paper, we examined one such tool, a hand held device used to measure alterations in tissue fluorescence. Loss of tissue autofluorescence has been associated with cancer and premalignant lesions at several sites, including the lung, cervix and oral cavity. Current evidence for utility of this device in identifying dysplastic lesions have found fluorescence visualization (FV) to be sensitive in the detection of high-grade dysplasias in the oral cavity (1), precancerous occult lesions (2) and in enhancing delineation of surgical margins (3, 4); however, these studies have all been done in high-risk referral clinic settings with experienced personnel. There are various reports of confounding factors such as inflammation, infection or highly pigmented areas which may cause a decrease in the FV signal and hence affect specificity (5–8).

This study evaluates the use of FV by community practitioners as an adjunct to clinical evaluation following a conventional examination. Our goal was to determine if FV added any value to white light oral cancer screening as introduced in the Guidelines for the Early Detection of Oral Cancer in British Columbia 2008 (9). The intent was to use this information to determine the value of this new technology in community dental practices and if suitable to develop a framework for knowledge translation and to test the hypothesis that FV is useful in facilitating the clinical decision to refer forward suspect lesions.

Materials and Methods

Study participants

This study was approved by the British Columbia Cancer Agency and the Simon Fraser University Research Ethics Board. Dental practitioners participating in this study were recruited using a notice in a Greater Vancouver dental association publication that described the study and requested volunteers. Each of these practices was contacted by telephone (DML) and was given a more in-depth description of the project and its timelines. A total of 18 dentists participated from 15 offices (2 offices had 2 dentists participating), with each dentist signing informed consent.

Data collection

The study included a one-day workshop to orient dental participants to the study protocols and subsequent follow-up of screening activities in each dental office, with facilitation and referral to dysplasia clinics for patients requiring further assessment.

Description of Workshop—The workshop was comprised of three parts. Firstly, before the start of the workshop, two short self-administered questionnaires, adapted from Yellowitz et al (10) and Horowitz et al (11) were completed to assess knowledge of oral cancer risk factors and to collect personal demographics on the participating dentists and information on their current screening activities. These findings will be presented elsewhere.

Secondly, a presentation was given, including a short review of oral cancer statistics, etiological factors, clinical risk factors and oral histopathology. An introduction to fluorescence visualization (FV), as an adjunctive device for lesion examination (1, 2) was

also given followed by a presentation of the step-by-step protocol for clinical assessment of patients, including extraoral and intraoral examination as described by Williams et al (12). Finally, the referral pathway for suspicious lesions and follow-up procedures were described.

Thirdly, the workshop concluded with a hands-on clinical session where each participant observed and performed an oral cancer screening examination of patients with active disease under both white light and FV conditions.

Assessment of oral cancer screening activities during follow-up of dental practices—After completion of the workshop, participants were asked to screen all patients over age 21 for the period from November 2007 to September 2008. Each practice was loaned a VELScope for the duration of the study (LED Dental, Inc., Burnaby, British Columbia, Canada). The study community facilitator (DML) then contacted each dental practice monthly for data acquisition and to address any questions on the study protocol. Participating offices were contacted regularly via email for the duration of the study. Each patient screened was given a unique identifier which was also used at the follow-up clinic and on further diagnostic reports, if required.

The dental offices were asked to complete the screening at each new patient or recall examination. The protocol included:

Step 1. Patient History: This step involved recording the patient's age, gender, personal and family history of oral cancer, tobacco use and alcohol consumption. The study questionnaire was developed as an adjunct to the dental offices' own medical history with the intent to minimize overlap and time spent by the clinician.

Step 2. Visual Screening Examination: This step involved both an extraoral and intraoral examination. The extraoral examination included inspection and palpation of the head and neck region, focusing on asymmetry and swelling or tenderness. Participants were asked to refer to a medical doctor any patient with fixed, firm or unexplained lymph nodes or asymmetries. An intraoral exam under incandescent (white light) conditions was then undertaken. If an anomaly was present, the site, colour, texture and appearance of the lesion was documented by checking off the appropriate boxes on a screening form and drawing the anomaly's location on an oral cavity diagram (Figure 1). Benign common mucosal changes not to be recorded included amalgam tattoos, Fordyce's granules, vascularities and pigmentation due to skin colour.

Step 3. Lesion Assessment: This step involved assessing the risk of an anomaly. Low-risk lesions (LR) included obvious trauma, aphthous lesions, melanotic macules, candidiasis (including median rhomboid glossitis) and geographic tongue. Anomalies without apparent cause, non-healing ulcers, red or white patches and lichenoid lesions were considered high-risk lesions (HR). Lichenoid lesions were later reclassified as intermediate-risk lesions (IR) because lichenoid lesions have a variation in clinical presentation from faint white striae to red and erosive and some may have increased cancer risk. Lesions in this latter group require further follow-up for clinical management.

Step 4. Direct FV: The FV component was the final step in the oral screening protocol. The FV examination followed the same methodical examination of all oral mucosa tissue as the conventional exam; however, it was done under reduced room lighting whenever possible and with a handheld autofluorescence imaging device, marketed as the Velscope™, (LED Dental, Inc., Burnaby, British Columbia, Canada). This device uses a blue/violet light (400 – 460 nm wavelength) to illuminate oral tissue, with long-pass and notch filters to allow

clinicians to directly view fluorescence (1, 13). Lesions that retained the normal green autofluorescence under FV were classified as FV negative (FV−); those that showed a reduction in the normal pale green, appearing as dark patches, were classified as FV positive (FV+). Where the clinician was unsure of FV loss, these lesions were classified as FV equivocal (FVE).

Participating clinicians were further asked to document sites which appeared clinically normal but had a loss of FV (FV+).

Lesion follow-up

Patients with low-risk (LR) lesions without an obvious cause, or with intermediate-risk (IR) and high-risk (HR) lesions were asked to return for reassessment in 3 weeks. If the lesion was still present after 3 weeks, the dental practice was requested to notify the study's community facilitator (DML) who reassessed the patient's lesion, both clinically and with FV, at the dental office. The community facilitator then referred any suspicious lesions to an oral medicine disease (OMD) clinic. In some cases, the dental offices directly referred patients to the OMD clinic. Oral medicine specialists at the OMD clinic determined if a biopsy or further follow-up was warranted.

Statistical analysis

Descriptive statistical analysis was used to describe data on knowledge and baseline screening behaviour of participating dentists collected at the initial workshop and on the patient screening forms. These latter forms were imaged and then uploaded directly into a Microsoft Excel study database using Teleform (version 10.1, 2006, Vista, California). Chi-squared tests were used to compare demographic and risk habit variables (Table 1), logistic regression models were used for Tables 2, 3, and 4; and the "Akaike Information Criteria (AIC)" was also used in Table 4 and 5. Data analysis was performed with SPSS software, version 16.0 for Windows, 2007 (SPSS Inc., Chicago, Illinois).

Results

A total of 2404 patients received a white light and FV screening examination and 357 patients with lesions (15% of patients) were identified. Of these lesions 192 were FV+ (54%), 26 FVE (7%) and 139 FV− (39%).

Demographic and risk habits

Table 1 displays the demographic and risk habit behaviour of study patients, comparing patients with lesions to those without a lesion. Lesions were significantly more likely to be found in patients who were older (40 years and older), smoked, consumed alcohol, and attended dental practices with larger clinic volumes.

Of the 357 patients with a lesion, age, gender, tobacco consumption (either smoking or chewing), alcohol consumption, lesion appearance, and risk of site were not associated with FV+ status (Table 2). Only the presence of colour and texture were associated with FV+ status. Red, or red and white lesions had a 5.6 fold (95% CI: 3.5 – 10.4) increased risk of being FV+. Lesion which were brown, black, or purple (common confounders such as amalgam tattoos, melanotic macules, nevi and vascularities) had a 2.8 fold (95%CI: 1.2 – 6.7) increased risk of being FV+. Many of these benign conditions are dark and hence, will provide a positive FV result. This emphasizes the importance of training in the use of FV and awareness of possible confounders. Lesions with a rough [RR=0.5 (95%CI: 0.2 – 0.9)] or 'other' [RR=0.3 (95%CI: 0.1 – 0.8)] texture were found to be significantly less likely to be FV+ than smooth lesions.

Impact of reassessment

Demographic, risk habit and clinical factors were also examined for an association with lesion persistence in the 141 patients called back for reassessment at 3 weeks. Six FV+ patients were referred directly to the oral medicine specialist without reassessment. Gender, age, tobacco consumption, alcohol consumption, risk of site, lesion appearance and colour were not found to be associated with lesion persistence in these patients. Only a rough lesion texture was associated with lesion persistence [RR=3.7(95%CI: 1.2 – 11.2)] (Table 3). Lesions which the dental professionals assessed as high risk (N=16) at the initial visit were also more likely to still be present at the 3-week reassessment visit than lesions assessed as low risk (N=121) [RR=2.7 (95%CI: 1.4 – 5.1)].

To see if FV and lesion risk assessment have the potential to predict lesion persistence, 4 different prediction models were compared (Table 4). Model 1 included all variable except for FV and lesion risk assessment, model 2 included FV, model 3 included lesion risk assessment and model 4 included both FV and lesion risk assessment. The 4 models were fitted with logistic regression and the relative risk was checked; this did not change substantively across the different models. For each model, -2Loglikelihood was reported and the AIC was generated. All 3 models (2, 3, and 4) are an improvement over model 1. There were significant differences between models 1 and 2, models 1 and 3, and models 1 and 4. The use of FV and assessing lesion risk are added to the model, both alone and together, increased the prediction of lesion persistence. Of the models 2, 3, and 4, model 4 has the lowest AIC and hence better predicts lesion persistence.

Of the 5 lesions that were biopsied all were persistent lesions, including 2 low-grade dysplasias. Only the melanotic macule was found to be FV− at reassessment, hence the brown colour of these lesions can be a confounding factor.

Experience of Clinician Training Effect

To assess if the results changed after the clinician became more experienced using the autofluorescence imaging device, the first 25% of all patients screened were considered a training set and removed from the total patients screened. The analyses were then repeated. Smoking and alcohol consumption were still significantly associated with the presence of a lesion, however, patient's age and dental practice clinic volume were no longer significant. FV+ status was associated with alcohol consumption and lesion colour (red, or red and white), while a rough texture was still associated with a FV− status. Both a rough texture and an intermediate- or high-risk lesion assessment were associated with the lesion persisting at the 3-week reassessment appointment. The results of the modelling remained the same (Table 5).

Discussion

In this study, we began the process of evaluating new technology in community dental practices, to ensure that such a technology transfer would be integrated into the conventional oral examination. Practitioners were introduced to FV during the workshop and supplied with a device for use in their practice. They were instructed to conduct an FV examination at the completion of each conventional white-light exam and to record observations made. As this was the first study to introduce FV technology into a community screening framework, our questions mainly focused on if positive FV results were associated with persisting lesions identified through a step-by-step procedure as described in the oral cancer screening guidelines (9). With training and experience we hypothesized that this device would add support to the reassessment and referral decision-making of community dental professionals.

The appearance of FV relies on three principles, the scattering of light as it interacts with tissue, the reflection of light from the tissue surface and the absorption of the light by the tissue components and re-emission as fluorescing light. How the light is absorbed, reflected or scattered depends on the biochemical composition of the tissue (14). Variation in light scattering may differ between individuals and by site (for example, the thicker epithelium of the buccal mucosa may reduce the back scattering of light as compared to the nonkeratinized epithelium of the floor of the mouth) (12, 15). Fluorophores are components of the tissue which absorb light at particular wavelengths and re-emit the light at longer wavelengths. They quickly become unstable and release the energy in the form of fluorescence which is very sensitive to cellular and tissue changes. Three fluorophores which react to the wavelength of light used with the FV autofluorescence imaging device are collagen and elastin found in the connective tissue and flavin adenine dinucleotide (FAD), a coenzyme involved with cellular metabolism (16). During carcinogenesis, the fluorescence intensity of collagen, elastin and FAD decreases (16).

Hemoglobin absorbs light and is more abundant during carcinogenesis as a result of increased microvascularization. However, hemoglobin also increases as a result of trauma or inflammation and is the main confounding factor, along with pigmented tissue, for FV (15, 17). Table 6 summarizes the tissue and cellular alterations which influence FV during carcinogenesis.

Previous studies with FV have been done in high-risk clinics. In a proof-of-concept study, FV was compared to histology. FV was able to distinguish high-grade dysplasia and squamous cell carcinoma (SCC) from normal tissue with a sensitivity of 98% and a specificity of 100% (1). High sensitivity in the detection of SCC has also been found by others, ranging from 84 – 100% (18, 19). The sensitivity in the detection of dysplasia is much lower, particularly in discriminating between benign and premalignant or malignant lesions (18, 19). A high rate of false positives has also been reported, however all data was collected at an initial visit. There was no follow-up visit to reduce the number of false positives that may have healed within a 3-week period and FV+ lesions were not followed longitudinally to see if there was progression. Hence, if FV reflects tissue alterations associated with progression; low-grade dysplasias which are FV− may not be at risk for progression (20).

In one study, FV was compared to white light examination by a nurse in patients with a history of head and neck cancer; a head and neck surgeon reviewed any abnormalities. No advantage was found for FV over a conventional white light examination. Autofluorescence identified the true positives; however, it had an increased number of false positives as compared to a white light examination. Approximately 25% of the lesions were not found in the oral cavity or oropharynx and, hence, may be difficult to visualize directly. It is unknown whether known confounders were excluded. Without follow-up, some of these lesions may be attributable to trauma or other temporary conditions and were not given an opportunity to heal. (21)

The value of experience using the FV autofluorescence imaging device along with reassessing patients was shown in our study. The strength of the models were increased when the training set was excluded and only the final 75% of screenings were analysed from each clinic.

While the use of FV has not, to date, validated itself within the general dental practice setting, it may increase the desire of oral health professionals to perform oral screening examinations and follow-up of patients with suspicious lesions.

There are several limitations of this study. Firstly, FV data was missing for the reassessment appointment. Clinicians may not have used FV at the reassessment appointment if the clinical lesion had resolved. Secondly, we were not able to biopsy all lesions for a definitive diagnosis due to ethical considerations. Thirdly, a clinical examination is subjective and varies with the experience of the clinician.

One of the most difficult decisions a clinician may face is when to refer a lesion for further investigation and biopsy. Recent evidence suggests high rates of clinical misdiagnosis by general oral health practitioners (22). For those clinicians in general practice without the experience and expertise of a specialist, an imaging device to aid in the decision to refer would be very helpful. At the community level, the critical decision is not whether or not the lesion is cancer but whether or not the lesion should be referred for further investigation. Reassessment at a 3-week follow-up appointment is critical to improving the specificity of the FV autofluorescence imaging device.

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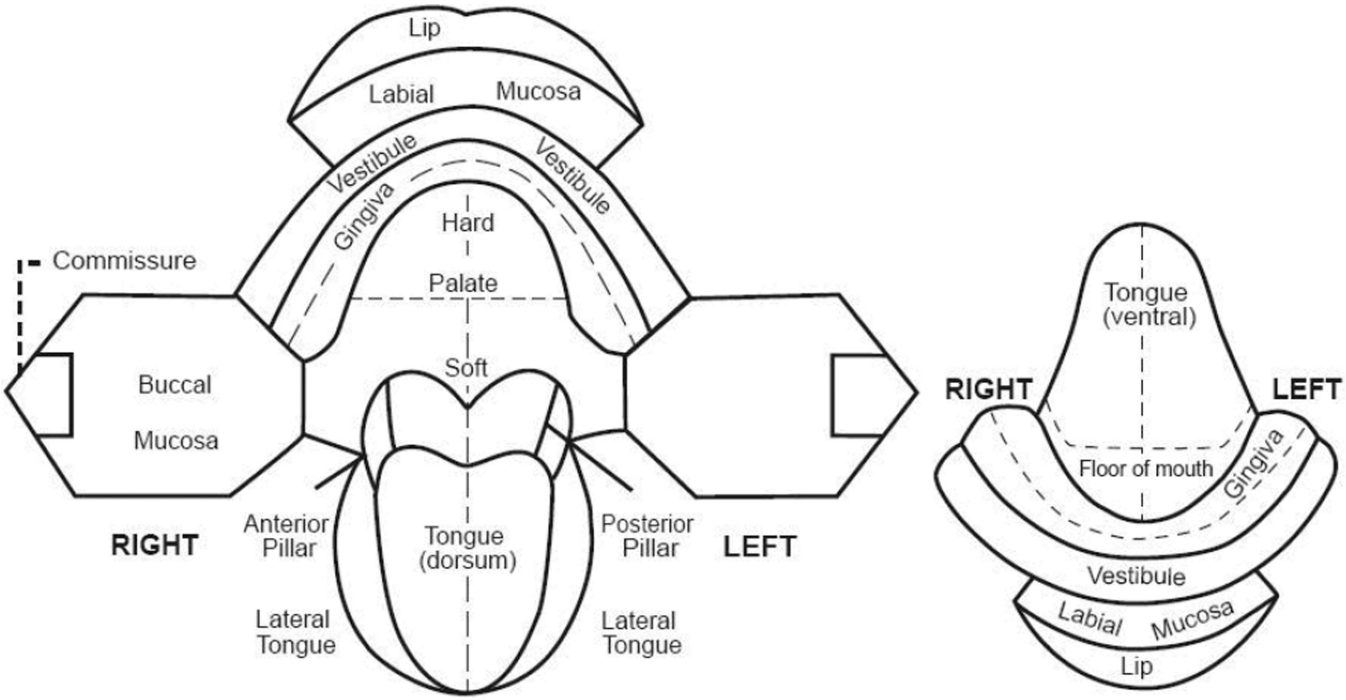

Figure 1.
Map of the oral cavity

Table 1

Demographic information and risk habit behaviours associated with an oral lesion of 2404 patients

	Lesion (%)	No lesion (%)	P value
Gender (N=2390)			
Male	165 (46)	857 (42)	0.164
Female	192 (54)	1176 (58)	
Age at screening (years) (N=2301)			
<40	58 (17)	458 (23)	0.006
≥40	288 (83)	1497 (77)	
Family history of oral cancer (N=2342)			
Yes	15 (4)	45 (2)	0.040
No	332 (96)	1950 (98)	
History of smoking (N=2343)			
Ever smoker[1]	166 (47)	764 (38)	0.002
Never Smoker	186 (53)	1227 (62)	
History of chewing tobacco (N=1824)			
Yes	9 (3)	32 (2)	0.277
No	278 (97)	1505 (98)	
Ever drinker (N=2352)			
Ever drinker[2]	234 (67)	1138 (57)	<0.001
Never drinker	115 (33)	865(43)	
Clinic volume (No. of patients screened per clinic) (N=2404)			
≤200	130 (36)	924 (45)	0.002
>200	227 (64)	1123 (55)	

[1] Ever smoker – smoked more than 100 cigarettes and longer than one year

[2] Ever drinker –drinks 2 or more alcohol drinks per week

Table 2

Demographic and clinical factors associated with FV+ status in 357 patients with an oral lesion

	FV+ (%)	FV− and FVE (%)	RR of a FV+ lesion (95%CI)
Gender (N=357)			
Female	106 (55)	86 (52)	1
Male	86 (45)	79 (48)	0.883 (0.582 – 1.341)
Age at screening (years) (N=346)			
<40	28 (15)	30 (19)	1
≥40	158 (85)	130 (81)	1.302 (0.740 – 2.291)
Family history of oral cancer (N=347)			
No	174 (94)	158 (98)	1
Yes	11 (6)	4 (3)	2.497 (0.779 – 8.001)
History of smoking (N=352)			
Never Smoker	95 (50)	91 (57)	1
Ever smoker[1]	96 (50)	70 (44)	1.314 (0.862 – 2.002)
History of chewing tobacco (N=287)			
No	152 (97)	126 (97)	1
Yes	5 (3)	4 (3)	1.036 (0.272 – 3.941)
History of drinking alcohol (N=349)			
Never drinker	54 (28)	61 (38)	1
Ever drinker[2]	134 (71)	100 (62)	1.514 (0.967 – 2.371)
Visible clinical lesion (N=353)			
No	25 (13)	32 (20)	1
Yes	166 (87)	130 (80)	1.634 (0.923 – 2.894)
High risk site (N=308)			
Low risk site	114 (63)	89 (70)	1
High risk site[3]	66 (37)	39 (31)	1.321 (0.815 – 2.142)
Appearance (N=229)			
Homogeneous	102 (75)	70 (76)	1
Nonhomogeneous	35 (26)	22 (24)	1.092 (0.591 – 2.017)
Colour (N=271) (P<0.001)			
White	20 (13)	50 (43)	1
Red or red and white	117 (76)	52 (44)	5.625 (3.048 – 10.382)
Other	17 (11)	15 (13)	2.833 (1.191 – 6.740)
Texture (N=257) (P=0.021)			
Smooth	93 (65)	52 (46)	1
Rough	25 (17)	30 (27)	0.466 (0.248 – 0.875)
Ulcer	17 (12)	16 (14)	0.594 (0.277 – 1.273)
Other	9 (6)	15 (13)	0.335 (0.137 – 0.820)
Lesion risk (N=357)			
Low risk[4]	175 (91)	150 (91)	1

	FV+ (%)	FV− and FVE (%)	RR of a FV+ lesion (95%CI)
Intermediate and high risk	17 (9)	15 (9)	0.971 (0.469 – 2.011)
Clinic volume (Number of patients screened per office) (N=357)			
≤200	67 (35)	63 (38)	1
>200	125 (65)	102 (62)	1.079 (0.858 – 1.355)

[1] Ever smoker – smoked more than 100 cigarettes and longer than one year.

[2] Ever drinker – drinks 2 or more alcohol drinks per week.

[3] High-risk site – floor of mouth, ventral or lateral tongue, soft palate.

[4] Confounders – trauma, candidiasis, geographic tongue, amalgam tattoo, varicosity, aphthous lesion, herpetic ulcer, melanotic macule.

Table 3

Demographic and clinical factors associated with lesion persistence in 135 patients who were reassessed at 3-weeks and with no missing values.

	Persistent (%)	Regression (%)	RR of a persistent lesion (95%CI)
Gender (N=135)			
Female	29 (58)	43 (51)	1
Male	21 (42)	42 (49)	0.896 (0.692 – 1.159)
Age at screening (years) (N=132)			
<40	4 (8)	10 (12)	1
≥40	45 (92)	73 (88)	1.155 (0.805 – 1.655)
Family history of oral cancer (N=129)			
No	45 (94)	73 (90)	1
Yes	3 (6)	8 (10)	0.851 (0.577 – 1.255)
History of smoking (N=133)			
Never Smoker	24 (48)	42 (51)	1
Ever smoker[1]	26 (52)	41 (49)	1.040 (0.799 – 1.354)
History of chewing tobacco (N=113)			
No	41 (98)	68 (96)	1
Yes	1 (2)	3 (4)	0.832 (0.464 – 1.492)
History of drinking alcohol (N=130)			
Never drinker	20 (41)	25 (31)	1
Ever drinker[2]	29 (59)	56 (69)	0.843 (0.623 – 1.141)
High risk site (N=123)			
Low risk site	26 (53)	36 (49)	1
High risk site[3]	23 (47)	38 (51)	0.932 (0.699 – 1.243)
Appearance (N=101)			
Homogeneous	23 (61)	47 (75)	1
Nonhomogeneous	15 (40)	16 (25)	1.301 (0.891 – 1.899)
Colour (N=112) (P=0.193)			
White	13 (30)	14 (21)	1
Red or red and white	23 (52)	47 (69)	0.527 (0.213 – 1.302)
Other	8 (18)	7 (10)	1.231 (0.348 – 4.358)
Texture (N=106) (P=0.073)			
Smooth	22 (55)	44 (67)	1
Rough	11 (28)	6 (9)	3.667 (1.198 – 11.223)
Ulcer	3 (8)	11 (17)	0.545 (0.138 – 2.158)
Other	4 (10)	5 (8)	1.600 (0.390 – 6.559)
Lesion risk (N=135)			
Low risk[4]	31 (62)	78 (92)	1
Intermediate and high risk	19 (38)	7 (8)	2.658 (1.396 – 5.062)
FV status (N=121)			

	Persistent (%)	Regression (%)	RR of a persistent lesion (95%CI)
FV− / FVE	35 (80)	55 (71)	1
FV+	9 (21)	22 (29)	1.61 (0.879 – 1.535)
Clinic volume (Number of patients screened per office) (N=135)			
≤200	22 (44)	40 (47)	1
>200	28 (56)	45 (53)	1.047 (0.808 – 1.355)

[1] Ever smoker – smoked more than 100 cigarettes and longer than one year.

[2] Ever drinker – drinks 2 or more alcohol drinks per week.

[3] High-risk site – floor of mouth, ventral or lateral tongue, soft palate.

[4] Confounders – trauma, candidiasis, geographic tongue, amalgam tattoo, varicosity, aphthous lesion, herpetic ulcer, melanotic macule.

Table 4

Persistence modelling[1, 2]

	Model 1	Model 2	Model 3	Model 4
FV +	-	3.407 (0.749 – 15.507)	-	2.771 (0.580 – 13.237)
Lesion risk (IR and HR)	-	-	7.560 (1.688 – 33.861)	8.208 (1.592 – 42.354)
−2 Log likelihood (df)	104.289 (11)	90.484 (12)	96.486 (12)	83.488 (13)
AIC[3]	115.289	102.484	108.486	96.488

[1] All models included gender, age at diagnosis, history of smoking, history of drinking alcohol, lesion appearance, colour and texture.

[2] Model 1 included all variables except for FV and lesion risk assessment, model 2 included FV, model 3 included lesion risk assessment and model 4 included both FV and lesion risk assessment.

[3] AIC - Akaike Information Criteria

Table 5

Persistence modelling results when using only the final 75% of patients in each clinic[1, 2]

	Model 1	Model 2	Model 3	Model 4
FV +	-	38.370 (1.474 – 999.136)	-	200.544 (1.220 – 32970.378)
Lesion risk (IR and HR)	-	-	36.834 (2.576 – 526.717)	1166.582 (1.765 – (770871.390)
−2 Log likelihood (df)	44.900 (11)	38.310 (12)	41.429 (12)	24.657 (13)
AIC[3]	55.900	50.310	53.429	37.657

[1] All models included gender, age at diagnosis, history of smoking, history of drinking alcohol, lesion appearance, colour and texture.

[2] Model 1 included all variables except for FV and lesion risk assessment, model 2 included FV, model 3 included lesion risk assessment and model 4 included both FV and lesion risk assessment.

[3] AIC - Akaike Information Criteria

Table 6

Tissue and cellular alterations which influence FV during carcinogenesis (23)

• Increased breakdown of collagen cross-links and the basement membrane by MMPs, including collagenase, causing less collagen fluorescence.
• Increased nuclear scattering due to changes to the cell nuclei resulting in less back scatter.
• Increased metabolism alters FAD and hence less fluorescence intensity.
• Increased microvascularity leads to more absorption by hemoglobin.
• Increased thickening of the epithelium leads to less reflectance and back scatter.