Oral Health Programme
Ministry of Health Malaysia

ORAL HEALTH TECHNOLOGY REVIEW

Visually-Enhanced Light Device For The Detection of Oral Potentially Malignant Disorders (OPMD) And Oral Cancer

1.0 INTRODUCTION

Oral cancer is the 11th most common cancer worldwide. Early detection of oral cancer is crucial in improving survival rate and quality of life.[1] Identification and detection of oral potentially malignant disorders (OPMD) allow delivery of early interventions to reduce the progression of these disorders to malignancy. The conventional practice for detection of OPMD and oral cancer is by direct visual inspection during oral examinations, followed by biopsy.[2] Currently, a variety of emerging hand-held diagnostic aids and adjunctive techniques are introduced to enhance clinician's ability to detect OPMD and oral cancer.[3] Light-based detection technologies commonly uses chemiluminescent or autofluorescent techniques. Chemiluminescent is the emission of light as a result of a chemical reaction. Autofluorescent is fluorescence emission observed when certain cell molecules are excited by UV or visible radiation of suitable wavelength around 365nm.

This technology review focuses on ViziLite® and Microlux™ DL, which use chemiluminescent technique (**Figure 1**) as well as VELscope® and Identafi®, which use autofluorescent technique (**Figure 2**). These devices have been adapted and marketed for the use in oral cavity.[4, 5] Their ability to highlight potentially malignant oral lesions in a highly sensitive and specific manner could potentially assist clinicians in early detection of oral cancer.

Figure 1 Chemiluminescent

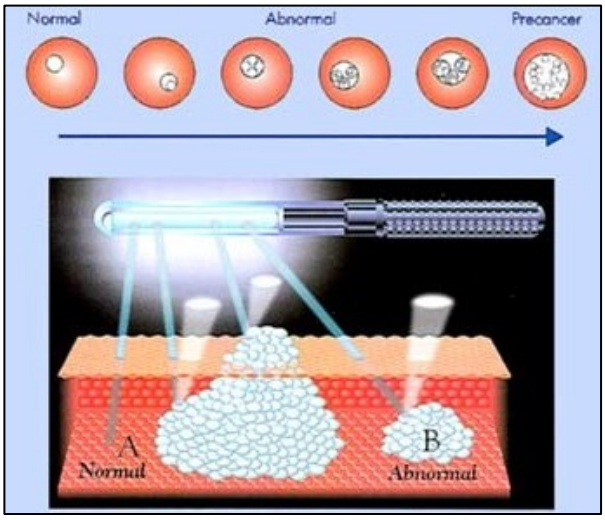
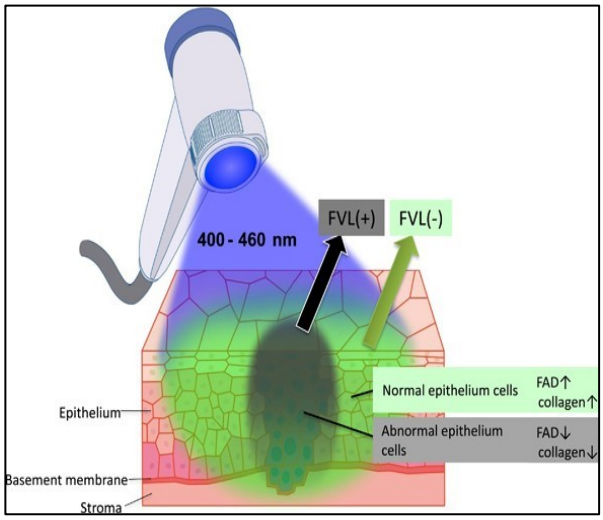


Figure 2 Autofluorescent



2.0 METHODS

The search for literatures were conducted via electronic databases, namely Ovid interface: Ovid MEDLINE, epub ahead of print, in-process, in-data-review & other non-indexed citations, daily and versions from 1946 to present; Cochrane Library: Cochrane Central Register of Controlled Trials August 2021; and PubMed. Google search engine was used to search additional web-based materials and information. Other relevant articles from references of retrieved articles were identified and reviewed. The articles retrieved were limited to English language and human studies. Terms used for search strategy were as follows:

1. MOUTH MUCOSA/ (27808)
2. ((oral or buccal or mouth) adj1 mucosa).tw. (18677)
3. MOUTH NEOPLASMS/ (36779)
4. cancer of mouth.tw. (49)
5. cancer of the mouth.tw. (327)
6. ((mouth or oral) adj1 (cancer* or neoplasm*)).tw. (14253)
7. PRECANCEROUS CONDITIONS/ (28522)
8. ((precancerous or preneoplastic) adj1 condition*).tw. (1380)
9. CARCINOMA, SQUAMOUS CELL/ (133418)
10. ((epidermoid or planocellular or squamous or squamous cell) adj1 carcinoma*).tw. (12449)
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 (216713)

12. velscope.tw. (70)
13. OPTICAL IMAGING/ (12459)
14. ((autofluorescence or fluorescence or fundus autofluorescence or optical) adj1 imaging*).tw. (23279)
15. FLUORESCENCE/ (44558)
16. fluorescence.tw. (339674)
17. EARLY DETECTION OF CANCER/ (29590)
18. (cancer adj2 (early detection or early diagnosis)).tw. (3992)
19. cancer screening.tw. (33618)
20. cancer screening test*.tw. (859)
21. (early adj3 (detection of cancer or diagnosis of cancer)).tw. (2626)
22. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (423030)
23. 11 and 22 (5386)
24. limit 23 to (english language and humans and yr="2011 -Current") (2574)
25. 12 or 13 or 14 or 15 or 16 (369707)
26. 11 and 25 (2873)
27. limit 26 to (english language and humans and yr="2011 -Current") (1040)
28. 11 and 12 (54)
29. limit 28 to (english language and humans and yr="2011 -Current") (35)

3.0 MECHANISM OF ACTION

In general, visually-enhanced light devices produce specific wavelengths of light to enhance visualisation of oral mucosal abnormalities that may not be visible to the naked eye. A light source with a different wavelength excites cells and promotes changes in spectral properties of the mucosa. The light-reflecting property of normal cells and light-absorbing property of abnormal cells allow visual distinction between the two tissues.[6] These hand-held light-based detection systems operate differently with its own unique features (**Table 1**).

Table 1 Visually-enhanced light devices.[3-5, 7, 8]

Name	Method of Use	Special Features
VELscope®	- Emits blue light to simulate natural fluorescence (wavelength: 400 - 460 nm). - Clinician views oral cavity through the device lens. - Normal tissue appears green, while abnormal tissue appears dark (reduction of green fluorescence).	- cordless, portable. - can be attached with digital camera. - no solutions required.
ViziLite®	- Uses low energy blue-white light source (wavelength: 430 - 580 nm). - Patient is required to pre-rinse for 60 seconds with 1% acetic acid solution. - Light source is activated by flexing a chemiluminescent light stick (vial container). It is then inserted into a holder. - Clinician views directly into oral cavity. - Normal tissue appears as dark blue, while abnormal tissue appears as acetowhite.	- cordless, portable. - can be used in conjunction with toluidine blue dye.
Identafi®	- Emits 3 type of light modes: white light mode (for routine oral examination), fluorescent violet mode (to identify abnormal tissue; wavelength: 405 nm), amber reflectance mode (to identify extent and vasculature around a lesion; wavelength: 545 nm). - Clinician views directly into oral cavity using the 3 modes sequentially. - Normal tissue appears fluorescent blue, while abnormal tissue appears dark brown or black.	- cordless, portable. - no solutions required.
Microlux™ DL	- Uses blue-white LED light source (wavelength: 430 - 580 nm). - Patient is required to pre-rinse for 60 seconds with 1% acetic acid solution. - Clinician views directly into oral cavity. - Normal tissue appears healthy pink, while abnormal tissue appears as acetowhite.	- cordless, portable.

4.0 EFFECTIVENESS / ACCURACY

Several studies and reviews have evaluated the accuracy of these devices in detecting OPMD and oral cancer (**Table 2**).

Table 2 Diagnostic values of visually-enhanced light devices.

Name	Sensitivity	Specificity
VELscope®	12.0% - 100% [3, 5, 6, 9]	15.3% - 100% [3, 5, 6, 9]
ViziLite®	7.1% - 100% [3, 5, 6]	0% - 78.0% [3, 5, 6]
Identafi®	12.5% - 50.0% [6, 8]	81.0% - 85.4% [6, 8]
Microlux™ DL	77.8% - 94.3% [5, 10]	70.7% - 99.6% [5, 10]

ViziLite® is found to be useful in enhancing the visibility of leukoplakia and provide distinct features from surrounding oral mucosa.[5] The examination requires a dark surrounding to increase visibility of acetowhite appearance. However, it was reported that ViziLite® is not a reliable tool to detect red lesions (erythroplakias), dysplastic lesions, oral squamous cell carcinoma (OSCC) and OPMD.[5, 7]

Both ViziLite® and VELscope® were reported to have high false positive rates (VELscope®; PPV= 6.4% - 58.1%; NPV= 57.1% - 100%)[9] (ViziLite®; PPV= 46.8% - 68.8%; NPV= 62.0% - 74.8%).[7] This could lead to overdiagnosis and contribute to high referral rate and over-treatment.[5, 7] VELscope® and Microlux™ DL are evidently effective in detecting presence of oral mucosal abnormalities, but not for distinguishing a simple acute inflammation, benign or malignant lesion.[6, 9] In other words, they can be used as adjunctive screening tools to detect oral tissue disorders, but not to discriminate the high-risk from low-risk lesions.[5, 9]

As for Identafi®, the white light mode enhanced visibility of oral mucosal lesions, but the violet light mode displays low sensitivity for detection of abnormal tissues. The green-amber light mode can provide additional clinical information on presence of diffuse vasculature, however, that should not be used to indicate underlying mucosal pathology. Therefore, this device should only be used as an adjunctive tool.[8] In general, conventional oral examination and surgical biopsy remain the gold standard in diagnosing OPMD and oral cancer.[5, 11]

5.0 COST

None of the studies measured cost-effectiveness of the light-based screening devices. Nevertheless, some studies suggested that ViziLite® would increase the cost of examination as the chemiluminescent vial is a one-time-use capsule for each patient.[5, 7, 12] Upon searching online, it was found that:

Table 3 Cost comparison of visually-enhanced light devices.

Name	Cost	Accessories Included
VELscope®	$1,695 (RM7,146)	charger, safety glasses, VELcap and VELsheath disposables, as well as brochures and training modules.[13]
ViziLite®	$307.87 per box (RM1,298.13)	each box consists of 10 vials.[14]
Identafi®	£2,370 (RM 13,709.59)	protective glasses, batteries and 100 disposable mirrors.[15]
Microlux™ DL	£324.50 (RM1,877.11)	starter kit which includes pre-rinse solution, protective sleeves and patient leaflets.[16]

6.0 REGULATIONS

In Malaysia, none of the visually-enhanced light devices is registered as medical device by Medical Device Authority.[17] On the other hand, all of these devices have been approved by the U.S. Food and Drug Administration (FDA) for use in the United States. Microlux™ DL was categorised under class I medical device, whereas the others were considered as class II medical device with the following indications (**Table 4**):

Table 4 Description of visually-enhanced light devices approved by FDA.[18]

Name	Approval Date	Intended Use
VELscope®	18 November 2010	- As an adjunct to traditional oral examination to enhance the visualisation of oral mucosal abnormalities that may not be apparent or visible to the naked eye. - To assist in identifying diseased tissue around a clinically apparent lesion and aid in determining the appropriate margin for surgical excision.
ViziLite®	31 January 2005	- As an adjunct to conventional oral mucosal screening for identification, evaluation and monitoring of oral mucosal abnormalities in an increased risk oral cancer population.
Identafi®	17 February 2009	- To enhance the identification and visualisation of oral mucosal abnormalities that may not be apparent or visible to the naked eye. - For conventional oral mucosal examination and excites the tissue with multispectral lights for direct visualisation of tissue and vasculature. - To help identify diseased tissue around a clinically apparent lesion and aid in determining the appropriate margin for surgical excision.
Microlux™ DL	4 April 2005	- As an aid to improve visualisation of oral lesions. - To be used in combination with a traditional examination by incandescent light.

8.0 CONCLUSION

Light-based detection devices are easy, safe, minimally time-consuming and non-invasive tools in detecting OPMD and oral cancer. They have shown to be useful in distinguishing between normal and abnormal tissues that are not apparent to the naked eye, but lack in ability to detect the different types of oral mucosal lesions and discriminate high-risk lesions. In consonance with extant reviews, there is inadequate evidence to draw valid conclusions on the effectiveness of visually-enhanced light devices as screening nor diagnostic tools. However, they may be used as an adjunct to conventional oral examination as they only possess adjunctive utilities. In any case, conventional oral examination followed by biopsy remain as the gold standard for early detection of OPMD and oral cancer.

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