



## PRELIMINARY DIAGNOSTIC AIDS USED IN ORAL CANCER

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### ABSTRACT

Oral cancer is a fatal disease and a major health issue in developing countries, which is the leading cause of death. Better understanding of the disease process at the molecular level has changed the way oral cancer approaches early diagnosis of the lesion rather than late stages to minimize morbidity and mortality. As a result, preliminary diagnostic aids have been suggested to improve our ability to distinguish between benign anomalies and dysplastic / malignant changes, and to identify areas of dysplasia / early oral cancer that are not visible to the naked eye. These include the use of vital staining, cytology, chemiluminescence, velscope etc.

**KEYWORDS:** Oral cancer, cytology, vital staining, chemiluminescence, velscope.

### INTRODUCTION

Oral cancer is the sixth most commonly occurring malignant tumor and is the leading cause of metastatic and invasive morbidity and mortality.<sup>[1]</sup>

It is regarded as an international health disease affecting the person health and lifestyle.<sup>[2]</sup>

Oral cancer is largely linked to lifestyle, with significant risk factors being tobacco and alcohol abuse. The use of smokeless tobacco was strongly linked to oral cancer in comparison to smoking. Oral squamous cell carcinoma (OSCC) accounts for nearly 40% of head and neck and 90-95% of oral malignancy.<sup>[4,5]</sup>

Changes in the oral mucosa occur, such as: white plaque, redness, ulcer or exophytic lesion, with no other signs / symptoms.<sup>6</sup> Five years of oral cancer survival ranges from 81% in patients with localized disease to 42% in patients with regional disease and 17% in patients with remote metastases.<sup>[7]</sup>

By total, less than 50 per cent of patients with oral and pharyngeal cancers live more than 5 years, according to late-stage diagnosis.<sup>[3]</sup>

Oral cancer care also results in speech impairment and distortion, mastication and chewing, and dental health. It can also affect the ability of the patient to interact socially, and must therefore be regarded as one of the most disabling and disfiguring cancers.<sup>3,8</sup> Unfortunately, early detection

of oral precancer and cancerous lesions has proven to be challenging, as the lesions are asymptomatic, doctors have a casual approach to harmless lesions and 50% of patients have area or distant metastases when diagnosed.<sup>[9]</sup>

The dental profession has developed an oral cancer screening device with increased technological advances that helps in early detection. An oral cancer screening device should be quick, easy and convenient.

### A Conventional Oral Examination (COE)

A conventional oral exam (COE), using natural (incandescent) light, has long been the standard method for screening for oral cancer. Oral cancer has to meet at least three of those criteria that has been identified.<sup>10,11</sup> An oral visual inspection carried out carefully by doctors and/or qualified health care workers under sufficient light will lead to early cancer detection and its precursors.<sup>12</sup> In different studies, sensitivity and specificity ranged from 58-94 percent to 76-98 percent respectively.<sup>[13,14]</sup>

### Cytology

Oral cytology has been broadly accepted as a method in early cancer diagnosis that has gained popularity within a short time since its introduction in 1942.<sup>15</sup> Cotton swabs were used in the earlier days to collect smears and wooden or metal spatulas followed. This method only extracts superficial layer cells, so that cell collection has improved. New technique using oral cdx cytobrush capable of non-invasively extracting basal layer cells and

assessing dysplasia through computer-assisted neural networks to remove subjective misinterpretation. However, many studies showed that the cytobrush has its limitations in sensitivity and specificity.<sup>[16]</sup> Using deoxyribo nucleic acid (DNA) cytometry, silver nucleolar organization regions (AgNOR), immunocytochemistry, and fluorescent in situ hybridization (FISH) will supplement the oral CDx method with full precision.<sup>[17,18]</sup>

#### **Vital staining**

Vital staining is usually simple, inexpensive, delicate, and efficient. It is a procedure where living cells take up certain dyes, which selectively stains some elements in the cells like mitochondria, lipid vesicles, lysosome, etc.<sup>[19]</sup>

#### **Toluidine blue staining**

Toluidine blue (TB) is a simple thiazine metachromatic colouring with a high affinity to acidic tissue components; thus, it stains nucleic acid-rich tissues. There are more nucleic acids in dysplastic and neoplastic cells than normal cells. In addition, malignant epithelium can contain intracellular canals that are wider than normal epithelium canals, facilitating dye penetration.<sup>[20]</sup> Sensitivity of this technique ranges from 0.78 to 1.0 while specificity yields to 0.31-1.0.<sup>[21]</sup> TB staining has a higher rate of identification of potentially malignant oral disorders and could further reduce the incidence of oral cancer compared with traditional visual inspection.<sup>[22]</sup> TB staining may however yield a high percentage of false positive outcomes. Many benign hyperplasia and inflammatory lesions may be black, as they contain large amounts of nucleic acids.<sup>[23]</sup>

#### **Methylene blue staining**

Methylene blue was first used in 2007 to detect lesions of the oral mucosa.<sup>[24,25]</sup> Methylene blue staining sensitivity 90-91.4 specificity 66.6-69. Similarly like TB, methylene blue also stains tissue with large quantities of nucleic acids.<sup>[26]</sup> Methylene blue staining is beneficial for screening high-risk individuals for oral cancer and is particularly sensitive to oral potentially malignant disorder detection.

#### **Rose bengal staining**

Rose bengal (RB) is the fluorescein-derivative of 4,5,6,7-tetrachloro-2,4',5',7'-. RB stain is commonly used for diagnosing ocular surface disorders.<sup>[27]</sup> It stains epithelial cells that are desquamated, dead or degenerated, but not healthy epithelial cells. Two studies have shown that RB staining could be a valuable diagnostic technique for detecting oral PMDs and oral cancer.<sup>[28]</sup> Rose bengal staining sensitivity 90-100 specificity 73.7-89.09.<sup>[29]</sup> RB staining has better result in revealing the dysplasia than toluidine blue because it can even detect mild dysplasia.

#### **Lugol's iodine staining**

The staining of iodine in Lugol is that iodine in the cytoplasm interacts with glycogen. The reaction, called the iodine-starch reaction, is visualized by a change of color. The loss of cell differentiation and increased glycolysis in cancer cells do not stimulate the iodine-starch reaction. Once applied to suspected lesions, natural mucosa stains brown or mahogany due to its high glycogen content, whereas lesions with dysplastic and cancer do not stain and appear pale compared to the surrounding tissue.<sup>[30]</sup> Studies were conducted on male Lugol's iodine staining 87.5-94.7 83.8-84.2 inmates, and suggested that it was highly effective as a screening tool for oral cancer in inmate populations.<sup>[31]</sup> The iodine staining of Lugol during surgery will assess margins of surgical resection, decrease local recurrence and increase survival in patients with epithelial dysphasia or malignant lesions.<sup>[32,33]</sup>

#### **Acetowhite staining**

It is relatively inexpensive and easy to use, interest has emerged in using acetic acid alone in the assessment of premalignant and malignant lesions. Acetic acid is used in the concentration of 3-5%. The color of positive result change to opaque white and no change or transparent white for negative result. It acts by causing dehydration of the cells, thereby producing a white appearance. It removed the mucus by coagulating and hence, allows the visualization of lesion. It also causes swelling of the epithelium and reduces its transparency by producing a transient coagulation of nuclear proteins. Thus, the higher nuclear content in premalignant and malignant lesions reacts with the acetic acid producing acetowhite appearance.<sup>[35,36]</sup>

#### **Light-based diagnostic aids**

A variety of light-based detection systems for detecting oral PMDs and oral cancer have been developed at their earliest stage. Mucosal tissues that undergo an irregular metabolic or structural change have different absorbance and reflectance profiles when exposed to different types of light sources, allowing oral mucosal anomalies to be detected.<sup>[37]</sup>

#### **Chemiluminescence**

Chemiluminescence for use in oral cavity is marketed under the names-Vizilite, Vizilite Plus, MicroLuxDL.<sup>[38]</sup> It is the light emission of a chemical reaction of varying degrees of severity of visual spectrum colors. The basic equipment involves the use of 1 min oral rinse with a 1% acetic acid solution accompanied by an oral mucosal examination under diffuse chemiluminescent blue / white light (490-510 nm wavelength).<sup>[39,40]</sup> The theory of this method is that the acetic acid removes the glycoprotein barrier and the oral mucosa is mildly dehydrated; abnormal mucosal cells then absorb and reflect the blue / white light different manner from normal cells. Natural mucosa appears blue, while unnatural mucosal areas emit light (due to the higher nuclear / cytoplasmic ratio of the epithelial cells) and look more acetowhite with lighter,

darker and much more distinct margins.<sup>[41]</sup> When viewed under a diffuse low-energy wavelength light, hyperkeratinized or dysplastic lesions appear clearly white.<sup>[42]</sup>

### VELscope

VELscope is designed as an alternative to traditional oral incandescent light testing by a dentist or health care practitioner in order to improve the identification of oral mucosal abnormalities that may not be visible to the naked eye, such as oral cancer or pre-malignant dysplasia. It is also used by surgeon for better identify the lesion tissue around thus help to determine the exact margin for procedure.<sup>[43]</sup>

Awan and Patil (2015) has conducted a systematic review of the literature to study the effectiveness of autofluorescence (VELscope) imaging systems for the diagnosis of oral premalignant and malignant lesion which has been reported improvement with VELscope in diagnosis of oral epithelial dysplasia.<sup>[44]</sup>

### CONCLUSION

Improving the identification and treatment of oral cancer has long been a major challenge for dental and health care providers around the world. Early detection and timely intervention is the essence of any cancer treatment protocol. Cancer screening includes looking for cancerous cells or pre-cancerous conditions before any symptoms occur and thereby protecting and avoiding this deadly disease. More studies need to be conducted using these diagnostic aids to determine the effectiveness and for early diagnosis of oral cancer.

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