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NON INVASIVE LIGHT BASED DIAGNOSTIC TOOLS FOR EARLY DETECTION OF CANCEROUS AND PRECANCEROUS LESIONS

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ABSTRACT

Oral cancer is one of the most common cancers that occur worldwide today. The five-year survival rate of oral cancer still remains low and most of the cases are diagnosed at later stages. Hence early diagnosis of suspected cases plays a major role. Several diagnostic aids are available in the market in recent years for early detection of oral potentially malignant disorders and early malignancies. The purpose of this article is to review the adjuvant non invasive light based diagnostic aids.

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INTRODUCTION

Head and neck cancer is considered to be sixth most common cancer worldwide and Oral Squamous Cell Carcinoma (OSCC) accounts for 40 % of head and neck cancer and 90-95% of oral malignancy (Mozafari *et al* 2012). Over 300,000 new cases of oral cancer are reported annually (Thomas *et al* 2013). In India, approximately 92,000 new cases of oral cancer are diagnosed every year and every 7 minutes 1 death occurs (Thomas *et al* 2013). If diagnosis is performed at stage 1 and 2 five-year survival is about 76% to 80%. Late diagnosis at stage 3 and 4 can reduce this percentage drastically to 41% and 9% respectively (Mozafari *et al* 2012). Lack of awareness among public regarding risk factors, various signs and symptoms are accounted for diagnostic delay in such cases (Masthan *et al* 2012). Hence, early diagnosis of suspected cases remains vital. Various newer diagnostic techniques have evolved to supplement the clinical examination and to improve the diagnosis of oral potentially malignant disorders and early malignant lesions. This review article focuses only on non invasive light based diagnostic aids.

Classification

Based on tissue reflecting property

- Vizilite
- Vizilite plus Tblue system
- Orasoptic DK

D. Microlux

Based on tissue autofluorescence property - VELscope

Based on both tissue reflecting and autofluorescence property- Identafi 3000 ultra

Tissue Reflecting Property

The absorption and scattering properties of oral epithelial tissues are reflected by their underlying physiological and morphological properties. In the visible light spectrum, the dominant light absorbers are haemoglobin (both oxygenated and deoxygenated) of blood vessels in the connective tissue stroma. The light scatters cell nuclei and organelles present in the epithelium and connective tissue, as well as collagen fibers and their cross-links. Neoplastic tissue exhibits significant changes in their physiological and morphological character which can be quantified optically. The scattering properties of epithelial layer are shown to increase with increased nuclear size, increased DNA content and hyperchromatism and that of connective tissue stroma are decreased due to neoplastic progression and collagen cross-links degradation. With angiogenesis the absorbing property of light is increased (Sandell *et al* 2011).

Vizilite

It is the chemiluminescent light source system first approved by FDA to improve the visualization of early cancer lesions (Trullenque *et al* 2009). The word "chemiluminescence" means

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production of light from a chemical reaction with limited emission of heat (Vashisht *et al* 2014). The Vizilite kit consists of a 1% acetic acid solution, a capsule, a retractor and an instructions manual. The capsule is formed by an outer shell of flexible plastic which may consists of acetylsalicylic acid and an inner vial of fragile glass with hydrogen peroxide. For the activation of light, the capsule is bent to break the glass vial so that the chemical products from the outer capsule and the inner vial react and produce a bluish-white light (wavelength of 430-580nm) which lasts for around 10 min (Trullenque *et al* 2009).

Following conventional examination, the patient is asked to perform a one minute mouth wash with 1% acetic acid which helps to remove the glycoprotein barrier, slightly dehydrate the oral mucosa and increases the visibility of nuclei of epithelial cell (Mozafari *et al* 2012). The ambient light is dimmed and a diffuse bluish-white chemiluminescent light is focused. Under this bluish- white light, normal cells absorb light and appear bluish and abnormal cells reflect the light and appear acetowhite with brighter and markedly distinguishable borders. This may be because of abnormal cells with increased nuclear cytoplasmic ratio and epithelium with hyperkeratinization and/or marked inflammatory infiltrate (Sambandham *et al* 2013). This system has Sensitivity and Specificity of about 77.3% and 27.8% respectively (Lingen *et al* 2008).

Vizilite system is simple, easy and non invasive technique helps the clinician for better identification of lesions and clearly demarcates its borders. However, this system cannot able to differentiate the lesion etiology – whether inflammatory, benign or malignant (Gaikwad *et al* 2013).

Vizilite Plus Tblue System

It is a modified technique containing Vizilite and Toluidine Blue Marking system which has received Food and Drug Administration clearance for visualizing the oral cavity as an adjuvant (Messadi *et al* (2013); Shashidara *et al* 2014). Toluidine blue also called as Tolonium chloride is a acidophilic metachromatic dye belongs to thiazine group selectively stains acidic components of tissue such as sulfates, carboxylates and phosphate radicals, thus staining DNA and RNA (Mendes *et al* 2011; Nagaraju *et al* 2010). It also stains dysplastic and anaplastic cells that contain quantitatively more nucleic acids than the normal oral mucosa (Nagaraju *et al* 2010). Also, the malignant epithelial cells may facilitate penetration of the dye more due to the presence of intracellular canals (Nagaraju *et al* 2010). Following conventional examination, the suspected lesion is examination under Vizilite. The acetowhite lesion visible under Vizilite is marked with toluidine blue marketing system provided by manufacturer. The lesion stained with toluidine blue is clearly visible even without light device and appropriate site for biopsy may be selected thereafter. With Vizilite Plus System, sensitivity is 100% and visualization of lesion is improved by 60% (Aggarwal *et al* 2011).

Orascope Dk

Orascope DK is a versatile, 3-in-1 device that has a battery-powered handheld LED light source and three interchangeable unique diagnostic instruments such as Oral lesion screening Instrument, Transilluminating Instrument and Lighted Mirror Instrument. The DK Transilluminating instrument helps to visualize crown fractures and caries in teeth with an intense,

focused beam of light. The DK Lighted Mirror has a powerful LED light source to illuminate the mirror's reflection which helps to increase visual acuity in inaccessible areas within the oral cavity. Oral lesion screening instrument helps in visualizing the oral lesions. The procedure is similar to Vizilite. The conventional examination is carried out in incandescent light. After 1%acetic acid mouth rinse, the oral cavity is reexamined with Oral lesion screening instrument which emits bluish white light The 'acetowhite lesions' appears brighter thereby helps to improve the visualization of lesions (Patton *et al* 2008; www.orascope.com).

Microlux DL

Microlux Diagnostic Light uses a battery-powered light-emitting diode (LED) fiberoptic source that generates a low energy blue-white light with the wavelength of 440-nanometer range. The procedure is similar to Vizilite and Orascope Dk. The advantage of this system is re- usable (Patton *et al* 2008; Ibrahim *et al* 2014). Microlux DL has the ability to enhance lesion visibility however, it is a poor in discriminating inflammatory, traumatic, and malignant lesions. This system has a sensitivity of 77.8% and a specificity of 70.7%, with a 36.8% positive predictive value (Mendes *et al* 2011).

Tissue Autofluorescence Property

This property has been used in the screening and diagnosis of precancer and early cancer of the cervix, uterine, lung, skin and more recently in the oral cavity also (Gaikwad *et al* 2013). Living tissues contain fluorophores such as NADH (Nicotinamide Adenine Dinucleotide), FAD (Flavin Adenine Dinucleotide), and collagen and elastin crosslinks in epithelium and sub mucosa, that produce fluorescence after excitation with specific light wavelengths (Gillenwater *et al* 2006; Yalcinakaya 2013). In dysplastic lesions of the oral cavity, there is the change in the structure and metabolism of the epithelium and submucosa, when interacting with light. The structural changes are thickening of the epithelium, hyperchromatism and increased nuclear pleomorphism, or increased microvasculature. The molecular changes are associated with the alteration in fluorophore distribution and breakdown of collagen and elastin matrix. These changes lead to increased absorption or scattering of light which reduces and modifies the detectable autofluorescence signal (Messadi *et al* 2013).

VELscope

VELscope is Visually Enhanced Lesion Scope. It is a handheld device approved by Federation Dentaire Association for assessing the autofluorescing ability of the oral cavity (Masthan *et al* 2012). The device consists of a light source and a visualizing handpiece through which suspect tissue is examined. The diagnostic ability of the device is based on the difference in the fluorescence property of normal and abnormal tissue within the oral cavity. With the help of blue-light excitation of wavelength 400–460 nm, normal oral mucosa emits a pale green autofluorescence when viewed through the filter incorporated within the hand-piece. Proper filtration is very much critical, as the intensity of the reflected blue-white light makes it difficult to visualize the narrow autofluorescence signal. Abnormal mucosa appears dark when compared with surrounding mucosa due to decreased level of autofluorescence (Yalcinkaya 2013). Thus, early biochemical

changes are detected even before it is clinically apparent, permitting the early detection of pathological changes (Trullenque *et al* 2009). It is safe, simple and the entire examination is completed in two minutes (Masthan *et al* 2012). The sensitivity of this device is ranged from 97% to 98% and specificity from 94% to 100% (Trullenque *et al* 2009).

Identafi 3000 Ultra

The Identafi is a multispectral screening device which incorporates three different lights white, violet and green-amber light which are designed to be used in a orderly manner to facilitate intraoral examination. This device uses both tissue reflecting and tissue fluorescence principle. First, the conventional oral examination is carried out in white light. Next the violet light with the wavelength of 405nm is used. This evaluates the autofluorescence properties of oral tissues through the accompanying photosensitive filters similar to VELscope. Finally, the green-amber light at 545 nm wavelength utilizes the concept of tissue reflecting property to delineate the vasculature in the connective tissue. Angiogenesis is an early step in carcinogenesis and there is a significant increase in microvessel count in mild and moderate dysplasia. Also there are tumour-induced angiogenesis which alters vascular morphology. This degree of change can assist in determining the prognosis of oral lesions. Thus evaluation of tissue angiogenesis in oral mucosal lesions enables the clinician to differentiate precancerous lesions from benign lesions (Bhatia *et al* 2013). According to the manufacturer, it is reusable. This device is its small size and easy accessibility to all tissues in the oral cavity when compared with VEL scope (Nagaraju *et al* 2010).

CONCLUSION

Even though various non-invasive light based diagnostic adjuvant are available, they lack in their effectiveness in detection of early precancerous and cancerous lesion. The biopsy with histopathological examination remains the gold standard. These devices are particularly useful for screening purpose as well as improve the visualization of clinically innocuous lesions.

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