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Spectroscopy in Screening of Oral Cancer and other Oral Lesions - A Review

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ABSTRACT

Cancer of the oral cavity is a major public health problem with approximately 300,000 new cases reported annually worldwide. It is known to develop from pre-existing potentially malignant oral lesions (PMOL) or de nevo. Most of the cases go unnoticed till they are in their advanced stage. The majority present with locally advanced disease (stage III and IV) with dismal 5-year survival rates of 20-50%. Persistent failure to diagnose and treat oral cancer at an early stage is a key factor limiting advances in the outcome. Improving detection, diagnosis, and treatment of precancerous changes and early asymptomatic cancers is imperative to increase survival and improve functional outcomes for persons at risk to develop oral cancer.

Keywords: *Spectroscopy, Oral Cancer, Diagnosis.*

1. INTRODUCTION:

Oral cancer is the world's sixth most common cancer, and global incidence and mortality rates are increasing.[1] However, oral cancer is predominantly a disease of developing nations, particularly prevalent in India and other south-east Asian countries due to the habit of tobacco usage. Although patients with the early disease have better chances for cure and functional outcome, most patients present with advanced tumors when treatment is more difficult, more expensive and less successful compared to earlier intervention.[2]. Conventionally it has relied upon visual examination and biopsy but inter-individual expertise in physical examination. as well as in histopathological confirmation, the demand for human and financial resources, the delay in time, amount of tissue gained via biopsy, and the obligatory invasiveness of a biopsy are factors affecting early diagnosis and thus adequate and initial treatment of cancer.[1] Oral squamous cell carcinoma (SCC) is one of the ten most common cancers worldwide. Despite therapeutic advances, survival rates for patients with oral SCC remain at approximately 50% and have not improved over several decades.[3]

2. CLINICALLY APPARENT ORAL PREMALIGNANT LESIONS

Genetic mutations often produce early phenotypic changes that may present as clinically apparent, recognizable lesions. An oral premalignant lesion (OPL) is an area of morphologically or genetically altered tissue that is more likely than normal tissue to develop cancer. Oral lesions that have been identified clinically as having the potential for malignant conversion include leukoplakia (a predominantly white lesion), erythroplakia (a predominantly reddish lesion), lichen planus, and submucous fibrosis. Reported rates of malignant transformation of leukoplakia range from less than 1% to 18% [3]. There is no accepted method to predict the risk of malignant progression of an individual OPL, but numerous factors such as location within the oral cavity, clinical appearance (homogeneous vs heterogeneous), and presence of dysplasia have been correlated with risk of progression. The histologic finding of dysplasia is strongly associated with an increased rate of invasive cancer development.[4]

3. LIGHT-BASED DETECTION SYSTEMS

Many light-based detection systems have been developed for the identification of oral PMDs and oral cancer at their earliest stage. Mucosal tissues undergoing abnormal metabolic or structural changes have different absorbance and reflectance profiles when exposed to various forms of light sources, enabling the identification of oral mucosal abnormalities.[5]

4. CHEMILUMINESCENCE

Commercially available chemiluminescence techniques include ViziLite, ViziLite Plus, Microlux/DL and Orascoptic DK. The main difference between these techniques is that ViziLite and ViziLite Plus involve a sole use chemiluminescent stick, while Microlux/DL and Orascoptic DX provide a blue-white light-emitting diode (LED) fiber-optic light. ViziLite positive lesions are abnormal oral mucosa. ViziLite shows high sensitivity in detecting oral PMDs and oral cancer.

5. VELSCOPE

The VELscope is a hand-held device that can enhance the visibility of oral mucosal abnormalities by activating tissue auto fluorescence. Auto fluorescence is due to the presence of endogenous fluorophores in cells, which produce a fluorescent emission when exposed to the light of a specific wavelength (Farah et al. 2012). At these excitation wavelengths, normal cells show a pale green fluorescence when viewed through a filter, while abnormal cells show a loss of auto fluorescence and appear dark. (Balevi 2007).
Some studies found that the VELscope can assist in screening for oral PMDs and oral cancer in populations at risk (Moro et al. 2010; Scheer et al. 2011).

In addition, several commonly occurring conditions, such as mucosal pigmentations, ulcerations, irritations, and gingivitis showed a loss of fluorescence under VELscope (Huber 2009).

6. PHOTODYNAMIC DIAGNOSIS

Photodynamic diagnosis (PDD) is based on the fluorescence generated by administration of an exogenous photoactivated compound that accumulates in cells with malignant potential, followed by appropriate photoirradiation (Uekusa et al. 2010). One of the most promising photosensitizers for oral PMDs and an oral cancer diagnosis is 5-aminolevulinic acid (ALA), which does not fluoresce itself, but can induce protoporphyrin IX (PPIX) fluorescence in tissue. Fluorescent tissues are considered suspicious for malignant transformation and biopsy should be considered (Driemel et al. 2007).

7. PRINCIPLE OF WORKING

Raman spectroscopy is based on analysis of in elastically scattered light. This technique has a wide range of uses in chemistry, solid-state physics, and other fields. Raman spectroscopy can distinguish between molecules and can identify them by their characteristic spectra .[6] Light can interact with matter in many ways and its response can yield useful information about the properties of the material. A good feature of light is non-invasive probing of the material when it is used at low intensities. This is especially important when we deal with human tissue. Another advantage is real-time data acquisition and processing. The diagnosis can be made on the spot. When light is incident upon a material, it can, in general, be reacted, absorbed, scattered or transmitted. When certain tissue starts to transform (e.g., cancerous cells begin to develop), its chemical composition often changes. If this change can be detected using Raman spectroscopy, the correct diagnosis can be made in the early stage of the disease. [6]

8. INSTRUMENTATION

Raman spectroscopy setup consists of three main components:

- excitation source (a laser)
- sample illumination and light collection system
- detection system

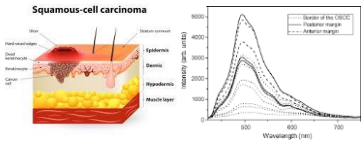
Figure 1, 2 and 3

Other clinical implications include Skin cancer diagnostics, Breast cancer diagnostics, Pre- malignant disorders, Oral Cancer etc.

9. ORAL CANCER

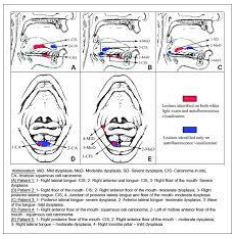
Alteration of healthy tissue into a malignant lesion is a gradual process which involves changes at the molecular level, thereby altering the morphology and tissue architecture. Cancer is an unusual growth of cells, which might conceivably attack the neighboring normal cells if left untreated.[7] inappropriate methods of cancer screening and diagnosis results in the delayed identification of the disease. [8]

Despite having accessibility to the oral cavity, most lesions are diagnosed in last stages of the illness, to be more precise unfortunately around 60 percent of them were in T3 or T4 by the time they were diagnosed. This indicates a critical impact on the survival rate, which is 40% according to the World Health Organization or less than 60% according to American Cancer Society.[9] In this scenario, Raman spectroscopy may prove to be a useful adjunctive tool for early diagnosis, which is of paramount importance to the long-term survival of patients. Raman spectroscopy in the identification of oral squamous cell carcinomas the malignant changes of which correspond to the increase in DNA and proteins. [10,11.] Raman spectroscopy is sensitive to a wide variety of proteins, lipids, and nucleic acids and has been applied in the analysis of various normal and diseased tissues
o progress during chemotherapy [12]. Guze et al. analyzed the tissue based molecular signatures of Raman spectra to differentiate the premalignant and malignant condition of normal mucosa and benign lesions, with the aim to overcome the subjective errors associated with histopathology.



10. APPLICATIONS OF RAMAN SPECTROSCOPY IN OTHER ORAL CONDITIONS

Sialoliths associated with the salivary glands and their ductal system are calcified masses usually composed of calcium phosphate (hydroxyapatite: [Ca10(PO4)6(OH)2)] with traces of magnesium and carbonate. These mineral components have been studied by various methods including high-resolution electron microscopy and X-ray diffraction. Kinoshita et al. explained in detail the precise formation of sialolith by analyzing the actual distribution of organic (amide III) and inorganic (phosphate) content within the sialolith with the help of Raman spectroscopy [13]. Yan et al. proposed a technique to apply Raman spectroscopy to examine the differences in the spectra between Warthin's tumor, pleomorphic adenoma, and normal parotid gland tissues [14].



11. CONCLUSION

Best way to improve outcomes is to improve early detection and diagnosis. Raman spectroscopy has been successful in differentiating normal tissue from the premalignant and malignant tissue. *In vivo* Raman spectroscopy has shown efficacy in the detection of normal tissue, pre- malignant disorders, cancer, and even of early changes such as cancer field effects or malignancy-associated changes in the oral cavity. However, the clinical applications of Raman spectroscopy have been limited by both the difficulty of capturing inherently weak tissue and the relatively slow speed of spectrum acquisitions.

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