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RESEARCH ARTICLE

VISUALLY ENHANCED LESION SCOPE –EARLY DETECTION IS THE KEY TO SURVIVAL

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ABSTRACT

Oral cancer is a potentially fatal disease with an increasing incidence and an unchanged five years mortality rate. The high mortality rate in cancer such as oral squamous cell carcinoma is commonly attributed to the negligence in detection of the disease at an early treatable stage. A number of promising recent technologies have been proposed to improve the effectiveness of early oral cancer detection. The world health organization has strongly identified prevention and early detection as one of the objectives in the control of oral cancers worldwide. The purpose of this article is to review the current knowledge about the commercially available diagnostic adjuncts in diagnosis of potentially malignant disorders.

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INTRODUCTION

Fluorescence visualization, Narrow emission technique, Light based detection technique, Auto fluorescence diagnostic test.

Oral and oro-pharyngeal cancers are a significant health problem throughout the world. Oral cancer is often deemed the "forgotten disease", because it kills more people than testicular cancer, cervical cancer and cancer of the brain each year. Certain chair-side diagnostic technologies and tests have entered the commercial market over the last ten years. Others are still being developed. A health practitioner visually examines the oral cavity with incandescent light, gauze, a mouth mirror, and magnification. Nearly all dental practitioners report that they regularly examine their patients for oral cancer, and yet only 15% of patients reported receiving an oral cancer examination on an American Dental Association Survey. There is no way to distinguish which lesions have the ability to transform into malignancies with a conventional oral examination alone (Ann Gillenwater, 1998). Conventional methods of detection of oral cancers include conventional biopsy, vital tissue staining, and cytological techniques. Toluidine blue (TB) staining is one of the most widely used, simple and inexpensive diagnostic procedure, which uses a blue dye to highlight abnormal areas of mucosa (Muralidaran, 2008). Recent advances for earlier ViziLite–ViziLite® system (Zila Pharmaceuticals, Phoenix, AZ) became the first system approved by the FDA to improve the visualization of early cancer lesions in head and neck examinations. VELscope allows dentists to meticulously screen for oral disease, picking up symptoms the naked eye can't see. It is a painless and non-invasive procedure that saves many lives every single year. Auto fluorescence spectroscopy is a new diagnostic modality with the potential to bridge this gap between clinical examination and invasive biopsy (Stefano Fedele, 2009 and Tsuimin Tsai, 2003). This review discusses about auto fluorescence techniques that available and developing adjuncts for early detection and diagnosis of oral cancer.

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Auto Fluorescence Spectroscopy

Tissue auto fluorescence in the screening and diagnosis of precancerous lesion in the lungs, cervix, skin has been already in the use for many years.[5] Loss of auto fluorescence in dysplastic and cancerous tissue is believed to reflect a complex mixture of alterations to intrinsic tissues fluorophore distribution due to tissue remodeling such as the breakdown of collagen matrix and elastic composition as well as alteration to metabolism such as the decrease in flavin adenine dinucleotide concentration and increase the reduction form of nicotinamide adenine dinucleotide associated with development of the disease (Meesadi, 2013). Auto fluorescence is an inherent property of biological tissues to fluorescence when suitably excited by UV or visible light due to the presence of biomolecule called fluorophores such as keratin, porphyrins, NAD(P)H, collagen and elastin. These natural fluorophores

undergo changesduring neoplastic progression. It is the natural fluorescence of the tissue itself. (Auto) to which no chemical substance has applied (Nathan kmle, 2012).

Principle

Different diseased tissue contains different morpho histological characteristics and intrinsic fluorophores that gives rise to different fluorescence emission spectra when the tissues are excited at a suitable wavelength. Normal oral mucosa emits pale green whereas abnormal tissue exhibits dark than the surrounding tissues (Nigam, 2014). The concept behind tissue auto fluorescence than changes in the structure like.

- Hyperkeratosis
- Hyperchromatic
- Increased cellular/ nuclear pleomorphism and metabolism of the epithelium.
- Changes of the sub epithelial storms alter their interaction with light.

Decomposition of collagen and elastin in the connective tissue layer, epithelial thickening and diagnosis plays major role in reducing intensity of auto fluorescence (Scilly, 2008).

Equipment

The spectroscopic system incorporates a fibro optic probe, 2 nitrogen pumped dye lasers and an optical multichannel analyzer. The probe consists of a central diver surrounded by 6 fibers and 3 fibers deliver excitation light at wavelengths of 337,365,410 nm. The other 4 fibers collect the fluorescence emitted from the tissue. The probe is disinfected before use and is then guided into the oral cavity and the tip illuminates laser light on the tissue surface and a quartz shield at the tip of the probe maintains a fixed distance between the fibers and the tissue. Collection fibers observe tissue fluorescence and emission spectrum is observed. According to the existing literature, the complete loss of the normal tissue fluorescence (fluorescence visualization loss) was rated as malignant or dysplastic. Fluorescence in red or orange was not rated as malignant according to the literature (Marle.w.Lingen, 2008).
In a study, 120 patients with suspicious oral premalignant lesions were examined with two examination methods. They were randomly divided into two groups. Group 1 was examined conventional with white-light and group 2 was examined additionally to the white-light-examination with an auto-fluorescence visualization device, VELscope. In a first step the two groups (only white light vs. white light and VELscope) were compared regarding baseline characteristics to exclude selection bias. Using biopsy as a gold standard, all patients were biopsied. The second step for the group examined with white light and VELscope, the diagnostic strategies were compared regarding sensitivity and specificity. The histological confirmation of lesions identified by using the adjunctive techniques and studies that specifically reported or presented data allowing calculation of the test's accuracy compared with the histologicalgold standard of tissue biopsy. Because of their acceptance by public health practitioners as the basic measures of accuracy of diagnostic testsand procedures, we identified sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The VELscope examination literally takes only two or three minutes. Initially, the dentist will perform a regular visual examination of the whole lower face. This includes the glands, tongue, cheeks and palate as well as the teeth. The dentist provides special eyewear to protect the integrity of the patient's retinas. The lights in the room are dimmed to allow a clear view of the oral cavity. Lesions and other indications of the oral cancer are easily noticeable because they appear much darker under the specialized light. If symptoms are noted, the dentist might take a biopsy to determine whether or not this is oral cancer. The results of the biopsy dictate the best course of action from there. Otherwise, another oral cancer screening is performed in one year's time.

Diagnostic Techniques

The auto-fluorescence based diagnostic techniques for oral cancer are:

- Visual auto-fluorescence (visually enhanced lesion scope [VELscope])
- Auto-fluorescence imaging
- Auto-fluorescence spectroscopy.

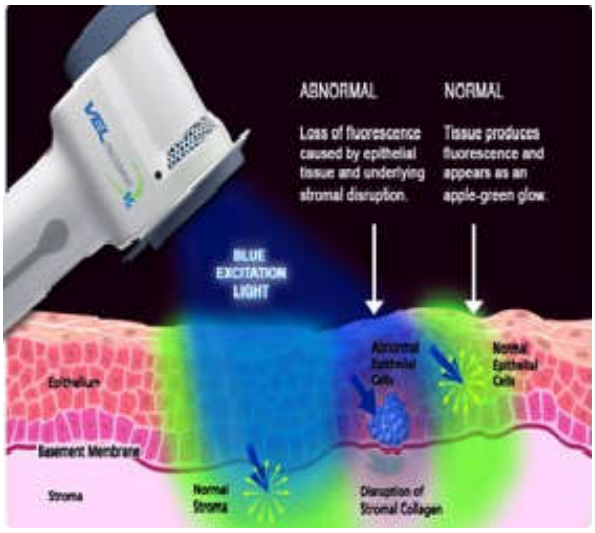

Fig. 1. Mechanism of action of Velscope

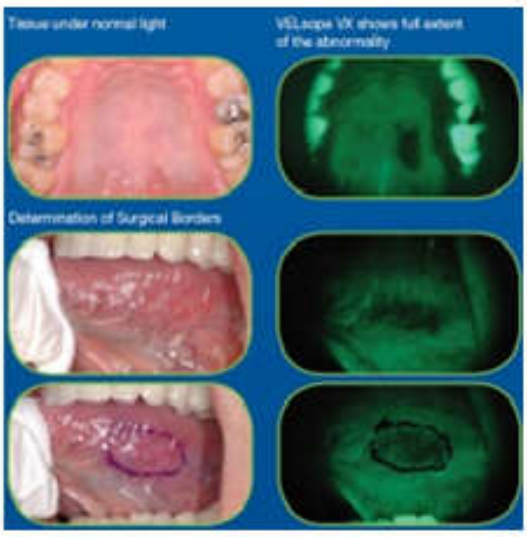

Fig. 2. Lesion depicting using Velscope

Visual Autofluorescence (Visually Enhanced Oral Lesion)

The visually enhanced lesion scope is a chair side diagnostic technique now marketed to a general dentist. It consists of a handheld device or scope which illuminated the mucosa with a

fluorescent light of wavelength 400 – 460 nm and a manual unit for direct visualization. Normal mucosa emits a green auto-fluorescence when exposed to this fluorescent light due to the presence of naturally occurring fluorophores in the mucosa. Abnormal mucosa appears dark due to the reduction or change in the quantity and quality of fluorophores in the mucosa which occurs due to abnormal or neoplastic changes of the mucosa. Many studies claim that VELscope improves the contrast between normal and lesion area, thereby easy identification of the lesion (Ruchika Khanna, 2016).

Autofluorescence Imaging

Auto-fluorescence imaging is a chair-side technique that can highlight a pre-cancerous lesion more efficiently than the normal white light examination. In this technique, tissues are illuminated with a light source, in the near Ultra-Violet to the green spectral range. The images of the fluorescence produced by the tissue are recorded using a camera. These images capture the alteration in the absorption and scattering events of the tissue. The captured digital images are used to interpret the lesion. Both normal and cancerous oral mucosa appears green in color. The neoplastic tissues possess low auto-fluorescence intensities when compare to normal tissue due to loss of stromal collagen. Thus, the neoplastic lesions can be demarcated from the normal tissue by a darker shade of green.

Auto fluorescence Spectroscopy

Auto-fluorescence spectroscopy is a rapidly emerging noninvasive technique that can detect the structural and chemical alteration in oral mucosa. Potentially malignant disorders and oral cancer are always associated with structural and biochemical alterations in the mucosa. Even before the clinical evidence of these lesions, molecular level change occurs. Compared to auto-fluorescence imaging, auto-fluorescence spectroscopy can detect even the minor alterations of the mucosa. This system consists of a light source usually in the near-Ultra-Violet to visible wavelength range that excites the tissue through a fiber. The fluorescence that is produced in the tissue is received with an analyzer probe. This probe can be disinfected with chlorhexidine gluconate and dried before use on a patient. Measurements were performed under a low ambient light level with the probe in contact with the oral mucosa. The obtained wavelengths are analyzed by a spectrograph. The recorded fluorescence spectra can be saved to a computer, which allows mathematical spectral analysis of many types. The light source used and the excitation wavelength performed in each study vary according to each investigator. There will be a decrease in fluorescence intensity and significant difference in the fluorescence intensities between the normal and neoplastic mucosa. In this, the patient performs a one-minute mouth rinse with the diluted acetic acid solution to remove the glycoprotein barrier and then the mucosa is dried. The intensity of ambient light is then dimmed and a diffuse bluish-white chemiluminescent light is applied. Normal cells absorb the light and have a bluish color, whereas the light is reflected by abnormal cells with a higher nucleus: cytoplasm ratio and by epithelium with excessive keratinization, hyper Para- keratinization and/or significant inflammatory infiltrate, which appear aceto-white with brighter, more marked and more distinguishable borders. Numerous studies have been conducted using VEL scope for the detection of premalignant disorders.

Gillenwater *et al* (1998) used autofluoresence to look at neoplastic and non-neoplastic oral mucosa and found that the fluorescence intensities were less for abnormal than normal sites. They showed that the ratio of red spectrum (> 600 nm) to the blue spectrum (455-490 nm) was greater in areas of abnormal disease with sensitivity of 88% and a specificity of 100% (Gillnetter19552). Onizawa *et al* (1999) used fluorescence spectroscopy for diagnosing oral cancer. 130 oral lesions from 130 patients were subjected to fluorescence spectroscopy. 72/79 (91.1%) of carcinoma and 6/7 (85.7%) of epithelial dysplasia were identified (Onizawa, 1996 and Onizawa, 1999).Van Staveren HJ *et al* (2000) used autofluoresence to distinguish oral dysplasia from normal mucosa using an artificial neural network and revealed a sensitivity and specificity of 86% and 100% respectively (Van Staveren, 2006) Sharwani A *et al* (2006) used fluorescence spectroscopy in combination with 5-aminolevulinic acid-induced protoporphyrin IX fluorescence in detecting oral premalignancy (Rahman,2010). mRahman *et al* studied autofluoresence between Normal and cancerous mucosa which had shown 90% of sensitivity and 87% of specificity. They concluded th at the technique was found as avaluable tool in the diagnosis of oral premalignancy. Thistechnique offers the potential to be advantageous over other nonoptical techniques intermsofprovidingreal-timediagnosis, non-invasiveness, absence of ionizing radiation, patient friendliness, repeatability.

Conclusion

The realm of oral cancer detection adjuncts and tests is an exciting and constantly progressing area of research and technology. Prevention of oral cancer is the key to survival and an oral cancer examination is essential for each patient every time they enter the dental office. Detection should lead to less damage from cancer therapy and to better prognosis. The VEL scope device, which uses visible light of 430nm wavelength to cause fluorescent excitation of certain compounds in the tissues, will play a major part in prevention of oral cancer diseases. Early detection and prompt treatment offer the best hope to the patient with oral cancer, providing the best chance of cure.

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