Review Paper:

Revolutionizing oral Cancer diagnosis: The impact of emerging medical technologies

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Abstract

Oral cancers are among the most frequent tumors in the world and oral oncology is a specialty area of medicine that focuses on their diagnosis, treatment and management. Prognosis and survival rates are greatly increased by early identification. A range of detection techniques such as advanced imaging technologies including MRI and CT scans, biopsies and ocular inspections are used. Furthermore, non-invasive possibilities for early detection are provided by recently developed techniques including optical coherence tomography and salivary diagnostics.

To improve the accuracy of detection, research is also being done on molecular and genetic markers. By combining these various approaches, oral oncology patient outcomes are eventually improved by thorough screening and prompt intervention.

Keywords: Oral Tumors, detection, autofluorescence examination.

Introduction

Oral cancer (OC) is defined as the growth of malignant tissue in the oral cavity, frequently affecting the tongue, floor of the mouth, cheek, gingiva, lips, or palate. Approximately 30% of cancer cases globally are in India and OC contributes to a third of every cancer diagnosis globally[5]. South-East Asia is home to most of worldwide cases of oral cancer, because of use of liquor and cigarette by population of this region. Approximately 90% of such malignancies are caused by oral squamous cell carcinoma (OSCC). Histologically composed of squamous cell populations that may exhibit various levels of distinction, OSCC constitutes an aggressive mucosal carcinoma[19].

The etiology of oral carcinoma often starts with symptoms such as a burning sensation in the mouth, difficulty in opening the mouth and the presence of red or white lesions in the oral cavity. Histological examination of these lesions may reveal dysplastic features. These conditions are classified as oral potentially malignant disorders (OPMDs). Early detection is crucial for a favorable prognosis and patient survival. Failure to identify OPMD in its early stages can lead to life-threatening consequences and increased morbidity[36].

Preventing fatality from premalignant oral cancers requires prompt detection as well as therapy. In the modern era, the most reliable methods for identifying malignant precursors and carcinoma of the mouth are an extensive medical evaluation of the mouth and biopsy. More precisely, oral lesions that remain for two weeks or longer despite eliminating potential topical allergens ought to get examined, as recommended by the WHO and the National Institute of Dental and Craniofacial Research[1].

The biosensors comprise receptor-transducer electronics that connect to an analytical substance through biological compounds[11]. By using a biological detection component, they can offer parametric or qualitative statistics. The development of biosensors is essential for identifying the biomarkers underlying these types of tumors and detecting OC promptly[33]. Biosensors have proven effective in detecting oral carcinoma (OC) early, with DNA, RNA and protein biosensors demonstrating their efficacy in non-invasive OC detection[21]. Electrochemical biosensors[10], surface plasmon resonance (SPR) sensors[34], surface-immobilized optical protein sensors[35] and lab-on-a-chip-based biosensors[24] are various types of biosensors used in early detection of oral cancer.

Due to the high sensitivity of autofluorescence examination, the fluorescence imaging device provides a simple, non-invasive screening test for oral mucosa which is useful in detecting high-risk oral lesions[17]. Autofluorescence occurs when endogenous fluorophores, such as certain amino acids, structural proteins and metabolic products, are excited by an external light source, emitting lower-energy photons as fluorescence. Significant fluorophores in the oral mucosa include nicotinamide adenine dinucleotide and flavin adenine dinucleotide, which emit specific wavelengths of light. Devices illuminating the oral mucosa excite these natural fluorophores, with mucosal abnormalities altering the tissue's absorption and scattering properties[15].

Optical Coherence Tomography: Optical coherence tomography (OCT) is a useful technique for producing pictures of the layered tissues by the measurement of backscattered light intensity which is depicted in figure 1. OCT ensures a depth of penetration ranging from 1 to 2 mm, contingent upon the tissues analyzed, as well as good axial and lateral resolution estimated at 13–17 and 17–22 µm respectively[28]. Oral squamous carcinoma may be detected early with the use of optical coherence tomography equipment, which has demonstrated the feasibility of evaluating the oral mucosa. Reliable determination of epithelial thickness *in vivo* and *ex vivo* is made possible by

OCT images, which offer information on the epithelium, the basal membrane and the lamina propria. OCT has proven to be able to identify several characteristics including basal membrane integrity and epithelial thickness, which have helped to determine whether the oral lesions are malignant. However, operator sensitivity in OCT image quality persists[8].

VELscope device: The 120-W metal-halide arc lamp in the bench-top casing of the VELscopeTM (Visually Enhance Lesion scope; MECTRON - European distributor for LED, Vancouver, Canada) device is paired with a handheld unit for direct observation, as well as a system of filters and reflectors optimized to produce near-UV/blue light between 400 and 460 nm. The patient wore protective eyewear throughout the treatment, which was conducted in a room with low lighting. The autofluorescence excitation device stimulates specific chemicals in the mucosa to glow by using visible light with a wavelength of 430 nm. The full loss of fluorescence in normal tissue (also known as fluorescence visualization loss) has been classified as malignant or dysplastic based on the literature that is currently available shown in figure 2.

Based on the available literature, a red or orange glow was not considered cancerous[2,27]. A lesion that is both VELscope-positive and light-absorbing needs to be closely watched. It is normally advised to get additional testing including a biopsy, if it does not go away after two weeks. Occasionally sampling benign tissue is considerably better than missing malignant or dysplastic lesions and being unable to identify them. In the fight against cancer, the VELscope improves our chances of early detection, which should result in fewer deaths from oral cancer[16,18].

Identafi 3000: To overcome the limitations of the VELscope, the Identafi 3000 combines three essential technologies: fluorescence imaging, fiber optics and confocal microscopy, to detect oral cancer[29]. This method measures tissue reflectance after being exposed to green-amber light (540–575 nm) as well as tissue auto-fluorescence using the VELscope technology[23]. It is thought that the green amber light source improves tissue reflectance quality, making the tissue vasculature easier to see.

It also helps to distinguish benign from malignant mouth lesions. High sensitivity of up to 82% and specificity of up to 87% are features of the Identafi 3000 system. Its effectiveness is attributed to its tiny size and significantly increased access to the oral mucosa tissue[30].

Oral Cancer Screening Using Microfluidics: Microfluidic devices, sometimes known as "Lab-on-a-chip," are capable of serving as an auto mated, smaller-scale replica of integrated experimental activities on a single device[38]. Microfluidic components for cell lysis, nucleic acid extraction, amplification and detection of a panel of mRNA obtained from a subset of cancer cells contained in a clinical specimen will be integrated into a comprehensive cancer diagnostics chip[22]. Its therapeutic utility for cancer treatment is improved by processing small sample biopsy samples or quickly, consistently and reliably assessing tumor biomarkers in biological fluids[6].

The effectiveness of employing a magnetic-bead-based microfluidic system to assess a patient's saliva for the presence of malignant or precancerous cells was assessed by Zoiber et al[38]. Moreover, information regarding the aberration in gene expression can be compared with data derived from normal cells using *in situ* lysis of the cells (using heat or osmotic shock) and mRNA extraction [38].

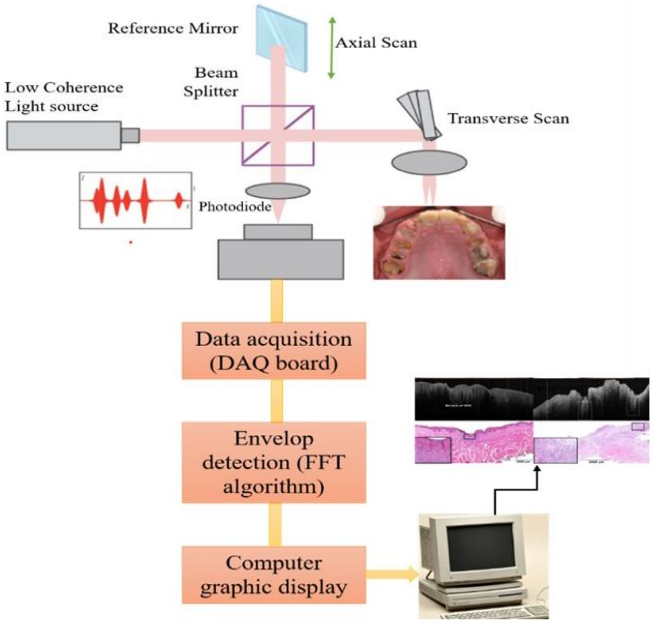

Figure 1: Mechanism of optical coherence tomography in oral tumors

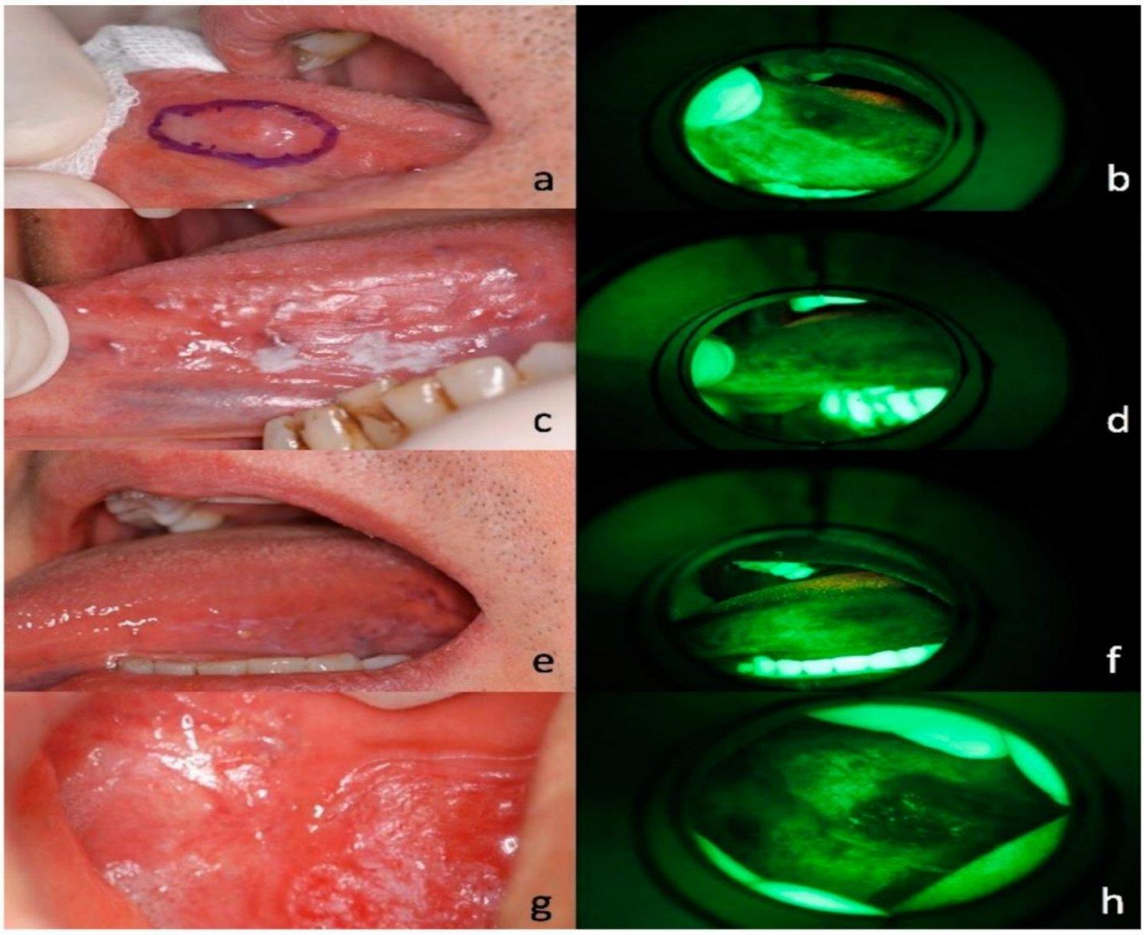

Figure 2: The illustration displays instances of loss of autofluorescence (LAF) on suspicious lesions that determined to be malignant upon histological testing using the VelScope examination method.
(a, b) A 58-year-old male smoker patient's nodular lesion of the left ventral tongue, as observed by VelScope examination, (c, d) A 47-year-old male patient's clinical appearance and VelScope examination of a single keratotic lesion of the left ventral tongue, (e, f) A 52-year-old male patient's keratotic and erythematous lesion of the left ventral tongue, observed by VelScope examination and (g, h) A 65-year-old female patient's clinical appearance and VelScope ecamination of an erythematous speckled lesion of the buccal mucosal[18].

Oral Cancer Detection Using Nanoparticles: The field of nanotechnology has advanced tremendously in the last few decades. Because nanoparticles (NPs) are so small (1–100 nm), they can easily be surface modified and they conjugate with biological molecules efficiently which makes them useful for a wide range of biomedical applications such as imaging, diagnostics and therapeutic agents[14,26]. There are gaps between endothelial cells in tumor blood arteries which are aberrant and extremely porous[9,13]. The enhanced permeability and retention (EPR) effect are the terms used to describe the potential of these macromolecules to specifically accumulate in the interstitial space of the tumor combined with a significant volume of blood plasma leakage and not be immediately removed[25]. At present, the majority of NPs are created using passive targeting to use the EPR effect in the detection and therapy of cancer.

Given the uncertainty surrounding the EPR effect within the tumor microenvironment, more precise and effective active targeting techniques are required. Consequently, to differentiate tumor-specific receptors, such as anti-epidermal growth factor receptor (anti-EGFR), NPS can be coupled with ligands or antibodies[7]. Better targeting results in less systemic toxicity and more effective delivery. In addition to the imaging-assisting contrast agents, NPs can also administer the active medication used in chemoradiotherapy and the photosensitizers (PS) used in photodynamic therapy (PDT)[4].

The metallic nanoparticles have been heralded as promising tools for accurate cancer diagnoses as well as multimodal therapy regimens due to their customizable absorption. Gold nanorods (GNRs) in particular show absorption in the near-infrared (NIR) spectrum[12]. Additionally, a range of nanoparticles (NPs) demonstrated distinct regulated optical, magnetic and electrical capabilities to produce heat and light for the treatment and diagnostics of oral cancer[37]. Further promising approaches for the diagnosis and treatment of cancer include gene therapy[32] and biosensors which are based on nanotechnology.

Because of their extremely tiny size, high reactivity and

tunable functional modification, nanoparticles (NPs) including both organic and inorganic ones, such as carbon nanotubes, polymeric NPs, liposomes and magnetic nanoparticles (MNPs), gold NPs and quantum dots (QDs)[3] have been employed extensively in various applications[20].

Conclusion

In conclusion, various detection methods for oral cancer including visual examinations, biopsy, imaging techniques and molecular diagnostics offer distinct advantages and limitations. Visual examinations and biopsies remain standard due to their direct and confirmatory nature, while imaging techniques like MRI and CT scans provide detailed insights into tumor extent and metastasis. Molecular diagnostics, encompassing biomarkers and genetic profiling, offer promising avenues for early detection and personalized treatment strategies.

Integrating these methods enhances diagnostic accuracy, enabling earlier intervention and improved patient outcomes. Continued advancements and combined approaches are essential for more effective and comprehensive oral cancer detection.

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