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Cancer stem cell and its niche in malignant progression of oral potentially malignant disorders

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Concurrent Oropharyngeal Squamous Cell Carcinomas in Couples

Prashanth Panta¹ and Mukund Seshadri²

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The publisher's final edited version of this article is available at <u>Oral Oncol</u> See the article "<u>Concurrent HPV-related oropharyngeal carcinoma in four couples</u>," in *Oral Oncol*, volume 86 on page 33.

Oral squamous cell carcinomas (OSCC) and oropharyngeal sequentity MNR lagar, Narsapur Road carcinomas (OPSCC) are distinct subsets of head and neck cancers, with the former predominantly attributed to carcinogen exposure (tobacco, areca nut, alcohol), and the latter, increasingly being linked to human papillomavirus infection. Several studies have linked sexual behaviors (number of lifetime sexual partners, oral sex partners) to elevated risk of OPSCC [1–3]. However, reports on HPV-related OPSCCs in couples also suggest a trend towards 'direct horizontal transmission' between intimate partners [4–9].

In this regard, Sathasivam *et al.* (Oral Oncology, 2018) have recently reported on concurrent HPV-related OPSCCs in four couples [9]. Although sexual transmission of HPV infection is well recognized, occurrence of HPV-related OPSCC in heterosexual couples is rare (5 couples reported in previous studies + 4 couples in the study by Sathasivam *et al.*). Whether this is a result of underreporting and/or likely to increase in the future remains to be seen. As for the risk of partners of OPSCC patients, work by D'Souza *et al.* suggests low prevalence of HPV oncogenic DNA (~1%) in partners of patients with HPV+ OPSCC [10]. It could be argued that other predisposing factors such as age, smoking could potentially contribute to the increased risk associated with horizontal transmission.



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Oral Cancer Screening: Application of Vital Stains as Adjuncts to Clinical Examination

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Abstract

An essential first line of investigation in oral oncology is clinical examination of high-risk oral sites. Given the elevated DNA content in cancers, vital dyes such as toluidine blue, methylene blue, Lugol's iodine, and rose bengal, which have an inherent chemical capacity to bind to DNA, have been studied for their clinical utility in screening malignant changes in the oral cavity in this chapter, we cover the basics of clinical examination and review the literature on the use of vital stars as adjunct disgnostic aids in patients with clinically subplicious oral lesions such as leukoplakis and enythroplakis. The goal of this chapter is to provide the reader with an overview of the vital stars available on the market and their potential for clinical application. A discussion of their strengths, limitations, and the rationale for development of new screening methods, has also been provided.

Keywords

Oral cancer Oral potentially malignant disorders Oral examination Vital stains Toluidine blue Methylene blue

Lugol's iodine Decision-making

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Optical Coherence Tomography: Emerging In Vivo Optical Biopsy Technique for Oral Cancers

Prashanth Panta, Chih-Wei Lu, Piyush Kumar, Tuan-Shu Ho, Sheng-Lung Huang, Pawan Kumar, C. Murali Krishna, K. Divakar Rao, and Renu John

Abstract

Oral cancers are a major health burden, and patients suffer from low survival rate owing to their late detection. Optical techniques are rapid, objective, and noninvasive methods with the potential to serve as adjunct screening/diagnostic tools, especially for cancers. This chapter highlights the advancements in oral cancer exploration using optical coherence tomography (OCT) with a discussion on basic principles of OCT, followed by a detailed description of oral cancer studies, subgrouped into animal studies, and ex vivo and in vivo human studies. We have included full-field OCT system-derived in vivo oral mucosa images in a healthy volunteer at different subsites showing standard microanatomy at vari-

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ous depths and also narrated some strategies to improve OCT results by multimodal approaches as well as through contrast enhancement for improved visualization.

11.1 Introduction

Optical coherence tomography (OCT) is a widely explored imaging modality that can provide highresolution, cross-sectional tomographic images of the ultrastructure of biological samples. OCT applications were reported in the early 1990s for noninvasive imaging of the retina [1, 2], and owing to its numerous advantages, it has been explored in a range of biomedical applications

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Salivary Biomarkers in Oral Cancer



Prashanth Panta and David T. W. Wong

Abstract

Saliva is an easily accessible biofluid with immense diagnostic potential in oral cancer. The identification of potential saliva signatures for early, noninvasive detection of oral squamous cell carcinoma (OSCC) lead to early detection, better outcome, and survival. More than 100 biomarkers have shown differential levels in saliva of patients with OSCC. They encompass a large number of proteins which cover cell surface molecules (CD44sol, CA-125, etc.), cytoskeleton fragments (CYFRA 21-1), intracellular proteins (ZNF-510, Mac-2 binding protein), proteases (MMPs) and inflammation-associated pro-

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teins (CRP, defensin-1, IL-6, IL-8), and mRNA signatures (IL-8, IL-1B, DUSP1, OAZ1, SAT, and H3F3A) and recently some noncoding RNA (miRNA and circular RNA). Some of these salivary biomarkers (both RNA and proteins) have displayed high sensitivity and specificity and were shown to reflect the underlying molecular characteristics and severity of OSCC. The salivary-mutated and salivary-methylated DNA, HPV-DNA, telomerase level, certain oral microbiota, metabolic and oxidative stress biomarkers, and inorganic ion concentration have also shown biomarker potential. Moreover, the unstable RNA is protected in exosomes, allowing their stable detection and easy quantification. The salivary transcriptome (coding, noncoding RNAs) has also displayed performance in multiethnic cohorts of oral cancer patients. In this chapter, the potential salivary biomarker signatures, corresponding tissue and serum concentration, and their role in OSCC are discussed.

14.1 Introduction

Oral cancer is the sixth most common malignancy in the world [1]. Oral squamous cell carcinoma (OSCC) accounts for ~90% of total oral cancer cases [1]. A significant portion of the global oral cancer burden occurs in the Indian subcontinent. Oral cancer progression is a multistep process

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Introduction to Oral Cancer

Prashanth Panta and Dimitrios Andreadis

Abstract

Oral cancer is the 6th most common type of human cancer with a 5-year survival rate approximately 50%, and its formation occurs in multiple steps. In the majority of cases, a well-established, preventable risk factor is involved. Several potentially malignant disorders precede oral cancer, each of them showing a well-defined clinical presentation. Spotting such precursor lesions should be no challenge to experienced clinicians. The 2017 World Health Organization (WHO) classification system on "oral potentially malignant disorders" is also presented here. Potentially malignant disorders encompass habit associated conditions, immune-mediated and inflammatory disorders, and also conditions that may arise due to solar radiation like actinic cheilitis and also genetic disorders like dyskeratosis congenita. Like in other cancer models, studies have focused on oral cancer stem cell population as the cancer-initiating cells and hidden culprits. Besides tobacco and alcohol, viruses (HPV), nutritional deficiencies, mechanical

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D. Andreadis, DDS, PhD Department of Oral Medicine/Pathology, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece trauma and galvanic phenomenon, candidal infection, and inherited mutations are now established etiological or synergistic factors that cannot be underestimated in the genesis and progress of oral cancer. This chapter deals with common risk factors and oral potentially malignant disorders.

1.1 Introduction

Oral cancer (OC) is the sixth common malignancy worldwide, but in India, the scenario is much worse, OC figuring as a leading cause of cancer [1]. Nearly 90% of OC cases are oral squamous cell carcinoma (OSCC), and most of them occur in individuals beyond 40 years, although recently trend is slightly different with more cases recorded among younger individuals [2]. The most common sites for OSCC are lateral border of the tongue, buccal mucosa, gingiva, and floor of the mouth. OSCC is often associated with well-defined risk factors. OSCC burdens millions of people worldwide and is mainly associated with tobacco, alcohol and areca nut, human papilloma virus, nutritional deficiency, mechanical trauma, and also infection with Candida spp. The majority of cases arise because tobacco and alcohol are complimentary. OC evolves from several precursor conditions and often is associated with a deleterious habit. Oral cancer may also arise from

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Genetics and Molecular Mechanisms in Oral Cancer Progression

Prashanth Panta, Bramanandam Manavathi, and Siddavaram Nagini

Abstract

Exposure to tobacco in smoke or chewable form, in isolation or in association with other risk factors (i.e., alcohol or areca nut), disturbs the balanced expression of numerous genes and leads to loss of coordination of their downstream signaling pathways, finally leading to oral cancer. Initially changes like mild dysplasia and benign hyperplasia are reversible, but continuous exposure to carcinogens leads to accumulation of mutations in multiple genes involved in cell proliferation, differentiation, apoptosis, telomere maintenance, invasion, and angiogenesis, resulting in abnormal cell behavior and cell immortalization. Gains and losses occur on many chromosomal arms, and a wellcharacterized mutational landscape is associated with oral cancer. This chapter discusses the wide spectrum of genetic and epigenetic events that take place in oncogenes and tumor suppressor genes with special reference to oncogenic

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S. Nagini, PhD Department of Biochemistry & Biotechnology, Annamalai University, Annāmalai Nagar, Tamil Nadu, India miRs (miR-21, miR-31, miR-146a, miR-134, miR-184, miR-7, miR-127, miR-518c-5p), tumor suppressor miRs (miR-200 family, miR-101, miR-26a/b, miR-29a, miR-27b, miR-137, miR-125a, miR-29a, miR-491-5p, miR-124, miR-125, miR-218, miR-99a, miR-375), and long noncoding RNA (HOTAIR, FOXCUT, MALAT1, UCA1, TUG1, CCAT2, FTH1P3, H19, HIFCAR/MIRHG) that influence oncogenic signaling pathways and enable acquisition of cancer hallmarks.

2.1 Introduction

Oral cancer, the sixth most common malignancy worldwide with an estimated annual incidence of over 300,000 cases and a mortality rate of 48%, presents predominantly as oral squamous cell carcinoma (OSCC) [1, 2]. The actiology of OSCC is multifactorial with interaction of a number of risk factors and host susceptibility. Tobacco consumption is the single most important risk factor implicated in OSCC development. Additionally, alcohol, viral infection, nutritional deficiency, dental hygiene, and socioeconomic and genetic factors are also recognized to contribute to OSCC development. Despite advances in prevention and treatment, the 5-year survival rate of OSCC remains low due to recurrence, chemoresistance, and lack of suitable markers for early detection [3]. An in-depth understanding of

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Dimitrios A. Andreadis, Achilleia-Maria Pavlou, and Prashanth Panta

Abstract

Oral cancer is a fairly common disease, which is unfortunately often diagnosed when it has reached an advanced stage. Early diagnosis is crucial for better prognosis and survival. In addition to better survival figures, early diagnosis also provides sufferers with a better quality of life. Biopsy is widely accepted as the "gold standard" diagnostic method for lesions raising suspicion of malignancy. There are several types of biopsy including incisional biopsy, excisional biopsy, fine needle aspiration, punch biopsy, and brush biopsy, each with specific indications, special methodology, advantages, and disadvantages. The use of biopsy and analyzing the results under the microscope is the gold standard for confirming a diagnosis of oral squamous cell carcinoma diagnosis. Biopsy is indicated in mucosal lesions (especially ulcers), and it is of

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P. Panta, MDS Department of Oral Medicine and Radiology, MNR Dental College and Hospital, Sangareddy, Telangana, India critical importance to reveal oral dysplasia, to confirm the clinical suspicion for an early invasive cancer, or to establish the grade of differentiation of oral squamous cell carcinoma for accurate therapeutic procedure and in the determination of prognosis.

6.1 Biopsy

6.1.1 Introduction

In 2012 there were 300,373 new cases of oral cancer worldwide as well as 145,353 deaths associated with this type of cancer. Tobacco and alcohol consumption constitute the main risk factors for oral cancer together with HPV infections, principally HPV-16 [1-3]. Oral cancer is initially often asymptomatic resulting in a delayed diagnosis. Early oral cancer diagnosis is crucial for a good prognosis, with patient survival being approximately 60-80% after early prognosis compared with 30-40% for late diagnosis and an advanced stage. An early diagnosis can also eliminate the need for extensive surgery and contributes to a better quality of life for patients [4-6]. Biopsy with a histological examination of the specimen is considered to be the "gold standard" diagnostic method for suspicious oral lesions. Its high reliability and its long history, more than 150 years, underpin this characterization [6-8].

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Oral Cancer Screening: Application of Vital Stains as Adjuncts to Clinical Examination

Prashanth Panta, Laurie J. Rich, and Mukund Seshadri

Abstract

An essential first line of investigation in oral oncology is clinical examination of high-risk oral sites. Given the elevated DNA content in cancers, vital dyes such as toluidine blue, methylene blue, Lugol's iodine, and rose bengal, which have an inherent chemical capacity to bind to DNA, have been studied for their clinical utility in screening malignant changes in the oral cavity. In this chapter, we cover the basics of clinical examination and review the literature on the use of vital stains as adjunct diagnostic aids in patients with clinically suspicious oral lesions such as leukoplakia and erythroplakia. The goal of this chapter is to provide the reader with an overview of the vital stains available on the market and their potential for clinical application. A discussion of their strengths, limitations, and the rationale for development of new screening methods, has also been provided.

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7.1 Introduction

Oral cancer is rampant in South-Central Asia accounting to 48.7% of total cases in 2012 [1]. India contributed to one-third of the global oral cancer burden (270,000 incident cases and 145,000 deaths) in 2009 [2, 3]. The morbidity and mortality associated with this disease presents a significant burden on health care. Histologically, over 90% of these cancers are oral squamous cell carcinomas (OSCC) and are associated with tobacco and betel nut use. Most oral cancer patients are diagnosed with advanced stage disease (stages III–IV) limiting their treatment options. Standard of care typically involves wide local excision and radical neck dissection.

Detection of oral cancer at an early stage (stage I or II) has a significant impact on the prognosis and overall survival of patients. For example, the 5-year survival rate for patients with OSCC of mobile tongue is 80% at stage I (local disease) and drops to 15% at stage IV [3]. Despite occurring in an easily accessible site, patients often present with advanced tumors at initial diagnosis. A majority of oral cancers present initially as oral potentially malignant disorders (OPMDs), and it is best to identify such precursor lesions to halt progression into invasive oral cancer. Although OPMDs have characteristic clinical presentation, some precancerous changes cannot be readily detected by visual examination under white light illumination. When a dentist or oral surgeon identifies a suspicious lesion, it is

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Keywords

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and narrow band imaging (NBI) instruments are among the optical imaging-based diagnostic platforms that are tools in oral oncology. These optical imaging techniques exploit differences in properties such as absorption. There has been widespread interest in the application of simple light-based methods and optical imaging as adjunctive chemiluminescence-based ViziLite® system, the Identafi® system that uses multispectral fluorescence and reflectance, to aid in tissue selection for biopsy. The autofluorescence-based Visual Enhanced Light scope (VELscope[®]), malignancy is often associated with a loss of fluorescence or fluorescence visualization loss (FVL) which may be used allows for deep tissue imaging and is actively being evaluated for diagnostic applications in oncology. In this chapter, we currently available for clinical use. In addition, photoacoustic imaging (PAI) is an advanced hybrid imaging method that tissue autofluorescence arising from endogenous chromatophores to detect malignant tissue. For example, early oral reflectance, and light scattering between normal and transformed epithelium. Optical imaging methods can also utilize their potential clinical applications. performance in oral oncology. The goal of this chapter is to provide the reader with an overview of these methods and will review the basics of these optical imaging methods and summarize preclinical and clinical evidence on their Ales

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Chapter

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Abstract



Colposcopy: A Direct Oral Microscopy for Oral Cancer and Precancer

Silvano Costa and Prashanth Panta

Abstract

Colposcope is a diagnostic tool frequently used in the practice of gynecology. Colposcopic examination is a painless procedure that is less time consuming and requires no anesthesia. The studies of this decade and a few from the previous one have shed light on the use of colposcopy in oral potentially malignant disorders and oral cancers. Cervical colposcopy is also associated with a few adverse outcomes which are not known to occur in oral colposcopy (direct oral microscopy) and the procedure does not vary much when applied to the oral mucosa. The colposcopic impression is mainly based on changes in the characteristics such as blood vessel caliber and pattern, spacing between capillaries, margins, color, and contour; however, for oral esions, the most important changes of value are the changes in vascular pattern. Direct oral miscroscopy is especially important in the selection of biopsy site. In this chapter a colposcopist and a stomatologist worked at the intersection to offer a basic

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P. Panta, MDS (四) Department of Oral Medicine and Radiology, MNR Dental College and Hospital, Sangareddy, Telangana, India e-mail: maithreya, prashanth@gmail.com knowledge of colposcopy practice in the arena it is routinely used, with a summary of the studies on oral oncology.

10.1 Introduction

Colposcopy is a diagnostic procedure developed in 1925 by H. Hinselmann, Director of the Gynecological Clinic of the University of Hamburg, Germany, for examining the uterine cervix and vagina in vivo, using a binocular magnification system with various magnification lenses and a light source. The word "colposcope" is derived from the ancient Greek word *colpos* which means "vagina." This procedure, conceived for the early detection of the pathological conditions of the cervix, is considered worldwide the most studied method for detection of early cervical neoplasia [1, 2].

The aim of colposcopy is to detect preneoplastic and neoplastic changes by analyzing the characteristics of the abnormal tissues such as (a) color, (b) morphology, (c) size, and (d) topography [3–5]. Comparison of these characteristics with established disease patterns allows the clinician to detect lesions and identify abnormal areas which may require a biopsy. Colposcopy is therefore an irreplaceable guidance exploration for pathology of the epithelium, be it cervical mucosa or oral mucosa. In the most recent times, colposcopy has been applied for oral cancers and oral

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Bioimpedance in Oral Cancer

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Gargi S. Sarode, Sachin C. Sarode, and Prashanth Panta

Abstract

Bioimpedance is described as the response of living organisms to an external current. It is an amount of obstruction to the flow of the external current through the tissues. Bioimpedance is a noninvasive method for evaluating the structure of a living organism. A bioimpedance signal can be used for describing the tissues. Bioimpedance of a tissue differs with different applied frequencies. It is an established technique in detection of breast cancer, cervical cancer, prostate cancer, and other cancers. There are evidences that significant differences exist between bioimpedance of normal and malignant tissue. With this view in mind, a comprehensive description of the technique is hereby given to deliberate the role of bioimpedance with a special emphasis on oral cancer. We have also discussed the studies carried out on oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC) and realized the necessity for more studies especially on OPMDs and OSCC together.

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12.1 Introduction

Impedance, by definition, is the effective resistance of an electric circuit or component to alternating current (AC), arising from the combined effects of ohmic resistance and reactance, or it is considered as a complex ratio of the voltage to the current in an AC circuit. It is the extent of the opposition that a circuit offers to a current when a voltage is applied. The word, impedance, was coined by Oliver Heaviside in 1886 [1]. Arthur Kennelly was the first to characterize impedance with complex numericals in 1893 [2]. Impedance encompasses the notion of resistance to AC circuits and retains both magnitude and phase, whereas resistance only has magnitude. The impedance caused by inductance and capacitance collectively denotes reactance and forms the imaginary part of impedance, while resistance forms the real part.

12.2 Bioimpedance

Bioimpedance is about the electrical properties of a tissue or a biomaterial. It simply means to what degree the tissue is a suitable conductor. It is the amount of how well the tissue opposes electric current course. It is the response of a living tissue to an externally applied electric current. It is an amount of the opposition to the course of current passing, as contrast to electrical conductivity. Thus, it is defined as the measurement of the impedance signal, which is

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13

Sensitive Crystallization Patterns in Oral Cancer

Sachin C. Sarode, Gargi S. Sarode, and Prashanth Panta

Abstract

Pfeiffer, a German scientist in 1938, first developed the crystallization test, which baffled many researchers ever since. Later on, cupric chloride crystallization test was widely used in the literature to investigate its efficacy in detection of various malignancies. Studies on oral cancer also proved its effectiveness for early detection. The crystallization appearance called "transverse form" is regarded as a hallmark pattern in malignancies. It is postulated that increased concentration of polyamines and diamines in blood of cancer patients as well as altered protein structure is responsible for formation of this peculiar, signature pattern. However, in normal healthy patients, the cupric chloride crystallization pattern is characterized by an eccentrically placed center of gravity and radiating crystals without any disturbances. In this chapter, we have reviewed the crystallization test with emphasis on potential mechanisms, crystallization test procedure and methodology, image interpretation, crystal patterns, and all studies

P. Panta, MDS Department of Oral Medicine and Radiology, MNR Dental College and Hospital, Sangareddy, Telangana, India e-mail: maithreya.prashanth@gmail.com conducted on oral cancer. The qualities of reliability, simplicity, cost-effective, and noninvasive nature of crystallization test make it an efficient tool for sensitive detection of oral cancer.

13.1 Introduction

Pfeiffer originally introduced the biocrystallization method in 1931, which was later termed "sensitive crystallization" and "copper chloride crystallization" [1]. This method involves crystallization of salt solution by evaporation of water under controlled atmospheric conditions. Differential pattern formation by virtue of interaction of biological material with molecular forces during crystallization is the basis of biocrystallization test [2]. It was used in agricultural research concerning crop quality, in addition to chemical analyses of vitamins, proteins, etc. [3]. A most common application is investigation of effects of different farming systems and fertilization practices on the morphological alterations found in the crystal structures [3-5]. It has also been applied as a bioassay in the field of homeopathy [6]. In the context of human diseases, crystallization method has been applied for renal diseases like pyelonephritis [7-9] and pulmonary conditions of the upper respiratory tract [10]. The application of sensitive crystallization processes in the early detection of malignancies is the most

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Saliva-Based Point-of-Care in Oral Cancer Detection: Current Trend and Future Opportunities

15

Prashanth Panta and David T. W. Wong

Abstract

Development of point-of-care (POC) for saliva-based, noninvasive detection of OSCC is an active area of research. Portable and easy-to-use biomedical devices and advanced electrochemical platforms (OFNASET) or simple paper-strip chromatography (e.g., OncAlert®), based on a single or a panel of salivary biomarkers, are already available for clinical use. In this chapter, the emerging core technologies and approaches assisting early POC detection are discussed. Knowledge from closely related fields like nanotechnology is also summarized to provide insight on

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possible future approaches that can be tailored for oral cancer detection. POC for oral cancer can be designed to work on a potential biomarker candidate (validated in multi-cohort and multiethnic studies) among the wide range of 100 signature analytes from proteins to RNA, cytomorphometry of exfoliated cells in saliva (analogous to circulating tumor cells in plasma), or through high-throughput screening of salivary exosomes for potential signatures. Surface-enhanced Raman scattering (SERS) was also used as a saliva assay previously, and such attempts will evolve significantly if saliva samples are mucin-free. ELISA is a common method for low-cost protein detection, with great POC potential. Its performance can be optimized through bead and nanoparticle technology. Sophisticated Luminex multi-analyte profiling (xMAP) technology and metal-linked immunosorbent assay (MeLISA), based on ELISA and biocatalytic ability of enzymes, were already reported with high sensitivity and specificity, which can be extrapolated to saliva samples. Some technologies have also assisted detection of mutations, such as "electric fieldinduced release and measurement" (EFIRM) recently deployed for identification of EGFR mutations through saliva samples. In this chapter, we have narrated the current trend and future opportunities for POC development in saliva-based oral cancer detection.

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Oral Oncology Volume 86, November 2018, Pages 316-317



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'Meditation Training Intervention' – A necessary shift for head and neck cancer patients

Prashanth Panta 53

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B.A. Rhoten et al.



Oral Oncology volume 85, October 2018, Pages 101-102



atten to the editor.

'Chronic traumatic ulcer of lateral tongue'- An underestimated 'oral potentially malignant disorder'?

Prachenth Panta 🔍 🖾 . Sachin C. Sarode, Gargi S. Sarode, Shankargouda Patil

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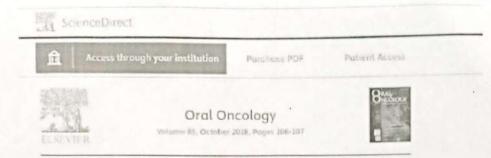
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Can healthy diet intercept progression of oral potentially malignant disorders?

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Proshanth Panta R. B. Sachin C. Sarade, Gargi S. Sarade, Shankargourda Patil

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Oral Oncology Sume 78, March 2018, Pages 218-219



New research directions for areca nut/betel quid and oral submucous fibrosis for holistic prevention and treatment

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Oral Oncology Volume 84, September 2018, Pages 126-127



Letter to the editor

Potential of web-resource on 'oral dysplasia and precancer'!

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Salivary Biomarkers in Oral Cancer

Prashanth Panta and David T. W. Wong

Abstract

Saliva is an easily accessible biofluid with immense diagnostic potential in oral cancer. The identification of potential saliva signatures for early, noninvasive detection of oral squamous cell carcinoma (OSCC) lead to early detection, better outcome, and survival. More than 100 biomarkers have shown differential levels in saliva of patients with OSCC. They encompass a large number of proteins which cover cell surface molecules (CD44sol, CA-125, etc.), cytoskeleton fragments (CYFRA 21-1), intracellular proteins (ZNF-510, Mac-2 binding protein), proteases (MMPs) and inflammation-associated pro-

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teins (CRP, defensin-1, IL-6, IL-8), and mRNA signatures (IL-8, IL-1B, DUSP1, OAZ1, SAT, and H3F3A) and recently some noncoding RNA (miRNA and circular RNA). Some of these salivary biomarkers (both RNA and proteins) have displayed high sensitivity and specificity and were shown to reflect the underlying molecular characteristics and severity of OSCC. The salivary-mutated and salivary-methylated DNA, HPV-DNA, telomerase level, certain oral microbiota, metabolic and oxidative stress biomarkers, and inorganic ion concentration have also shown biomarker potential. Moreover, the unstable RNA is protected in exosomes, allowing their stable detection and easy quantification. The salivary transcriptome (coding, noncoding RNAs) has also displayed performance in multiethnic cohorts of oral cancer patients. In this chapter, the potential salivary biomarker signatures, corresponding tissue and serum concentration, and their role in OSCC are discussed.

14.1 Introduction

Oral cancer is the sixth most common malignancy in the world [1]. Oral squamous cell carcinoma (OSCC) accounts for ~90% of total oral cancer cases [1]. A significant portion of the global oral cancer burden occurs in the Indian subcontinent. Oral cancer progression is a multistep process

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Optical Coherence Tomography: Emerging In Vivo Optical Biopsy Technique for Oral Cancers

Prashanth Panta, Chih-Wei Lu, Piyush Kumar, Tuan-Shu Ho, Sheng-Lung Huang, Pawan Kumar, C. Murali Krishna, K. Divakar Rao, and Renu John

Abstract

Oral cancers are a major health burden, and patients suffer from low survival rate owing to their late detection. Optical techniques are rapid, objective, and noninvasive methods with the potential to serve as adjunct screening/diagnostic tools, especially for cancers. This chapter highlights the advancements in oral cancer exploration using optical coherence tomography (OCT) with a discussion on basic principles of OCT, followed by a detailed description of oral cancer studies, subgrouped into animal studies, and ex vivo and in vivo human studies. We have included full-field OCT system-derived in vivo oral mucosa images in a healthy volunteer at different subsites showing standard microanatomy at vari-

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Graduate Institute of Photonics and Optoelectronics, National Taiwan University, Taipei, Taiwan ous depths and also narrated some strategies to improve OCT results by multimodal approaches as well as through contrast enhancement for improved visualization.

11.1 Introduction

Optical coherence tomography (OCT) is a widely explored imaging modality that can provide highresolution, cross-sectional tomographic images of the ultrastructure of biological samples. OCT applications were reported in the early 1990s for noninvasive imaging of the retina [1, 2], and owing to its numerous advantages, it has been explored in a range of biomedical applications

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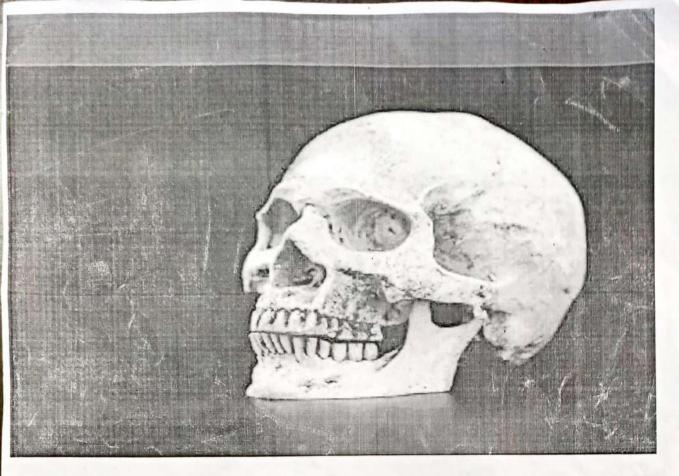
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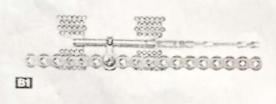
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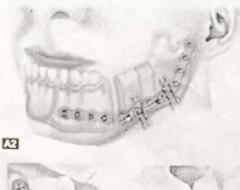
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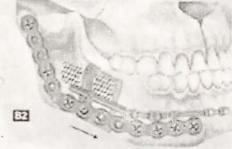


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