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## RESEARCH ARTICLE

### RECENT ADVANCES IN DIAGNOSTIC MODALITIES OF ORAL CANCER

**1,\*Abhimanyu Sharma, 2Sanjiv Nair, 3Shibani Grover, 4Pritham Shetty and 5Lokesh Chandra**

<sup>1</sup>MDS, Research Associate, Oral Surgery, ESICDC, New Delhi

<sup>2</sup>Professor & HOD, Oral Surgery, BIDS, Bangalore

<sup>3</sup>Director Professor & HOD Endodontics, ESIC Dental College, New Delhi

<sup>4</sup>Professor, Oral Surgery, BIDS, Bangalore

<sup>5</sup>Associate Professor, Oral Surgery, ESIC Dental College, New Delhi

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#### ABSTRACT

Cancer is one of the leading cause of death worldwide. Oral cancer is highly prevalent in south Asian countries. Delay in diagnosis of the same eventually lead to delay and complexity in treatment plan with compromised results and reduction of survival rate of patients. Patient awareness stands as a huge factor in early and proper diagnosis of cancer. Sometimes even on timely reporting of a questionable lesion it may not get diagnosed exactly due to highly operator dependent reporting of the results. It is the need of time to get these lesions diagnosed not just at an early stage but also with higher rates of true positive results. Various recent advanced in the field of diagnosis of oral cancers appears to be promising but still are unpopular.

#### INTRODUCTION

Most of the oral cancer remains undiagnosed until the disease is well advanced with presence of metastasis. With the efforts and developments in field of science there is an obvious advancement in diagnostic modalities available for screening and early detection of oral cancer. Early detection of oral cancer will not just improve the prognosis by treating the same at an early stage, reduce the complexity and complications of treatment, but will also reduce the monetary burden on patient. Available Screening and diagnostic options are Tumor markers (Genetic analysis), Biopsy (Histopathological analysis) and Diagnostic scans such as CT and MRI which have their own limitations, chances of giving false negative results and hazards respectively. It is well known that the treatment plan and thus prognosis of oral cancer depends upon the stage of disease and time of diagnosis. There is a direct relation between the stage at time of detection and five year survival rates. Most of the common diagnostic modalities used today viz Biopsy, CT Scan, MRI have their own limitations and evaluation of the findings, up to an extent depends upon the skill and expertise of the pathologist or radiologist.

Sometimes these modalities may give a false negative result. As document in recent studies, The latest techniques are mostly non invasive and are capable of diagnosis oral cancers and potentially malignant lesion at an earlier stage with significantly higher sensitivity and specificity.

**Elucidation:** Saliva Recent trials on saliva serum testing for proteomic and genomic structures such as enzymes, cytokines, growth factor, metalloproteinase, cytokeratins and ribonucleic acid transcripts proved to be effective as a non invasive alternative for diagnosis of oral cancer<sup>1</sup>.

**Lugol's Iodine:** This dye can be used for detection and marginal delineation of Oral squamous cell carcinomas and dysplasia. It is a safe and non invasive alternative which shows and differentiate the dysplastic changes from normal tissue but variation in uptake of dye<sup>2</sup>.

**Toluidine blue:** Many studies in the past have shown the success of toluidine blue in detection of oral cancer by distinguishing tumor margins. If not as a tool by itself, it can at least aid in selection of the biopsy site. Literature showed High sensitivity of the same in detection of oral cancer. Studies have also suggested that Toluidine blue is more sensitive in detecting carcinomas proper, than dysplasia<sup>3</sup>.

\*Corresponding author: Abhimanyu Sharma,  
MDS, Research Associate, Oral Surgery, ESICDC, New Delhi.

**Brush biopsy analysis by MALDI-ToF Mass Spectrometry:**

A recent study by Maurer (2013) proposed that Intact cell peptidome profiling using MALDI-ToF Mass Spectrometry is able to distinguish not just between healthy and cancerous mucosa but also between other oral lesions and oral cancer with excellent sensitivity and specificity which may lead to more accurate early diagnosis. Brush biopsy is a known diagnostic tool for detection of dysplastic changes but it depends on the accuracy of pathologist. In this technique the authors used profiling of intact cell peptidomes using matrix assisted laser desorption/ionization time of flight mass spectrometry. The basis of this technique is the genetic alterations that takes place when a healthy cell matures into a tumor cell.<sup>4</sup>

**FTIR Spectroscopy:** A very recent paper discussed about role of Fourier transform infrared (FTIR) spectroscopy which can also be explained as a biochemical fingerprint. It works on the principle of absorption of Infrared rays by those molecules whose vibration frequency is same as that of the directed IR rays and thus defining the structure of molecule. FTIR is able to measure biochemical changes in tissue specimens and thus is able to differentiate between normal tissue and tumour tissue.<sup>5</sup>

**Tissue fluorescence spectroscopy:** This method uses optical fibre for autofluorescence spectroscopy that generates modulated wavelengths and these excited wavelengths are than recorded and interpretate changes in tissue fluorescence. As of now it is used only as a subordinate tool for the study of already diagnosed lesions.<sup>6</sup>

**Serum Profiling:** Serum profiling have shown the changes in levels of few minerals, antigen and immune complex in oral cancer patient. A study showed significantly lower iron and selenium levels and higher copper levels in oral cancer patients. Its reliability as a diagnostic tool is limited and questionable due to poor diagnostic sensitivity and specificity<sup>7,8</sup>.

**Gold Nanorods:** In a study by Hong Wang et al a Rose Bengal conjugated gold nanorod (RB-GNR) platform was developed for optical detection of cancer cells. The GNRs were modified by poly(allylamine hydrochloride) and conjugated with RB molecules to produce RB-GNRs which exhibit strong optical absorption in the nearinfrared (NIR) region. Based on the NIR absorption by the RB-GNRs specifically conjugated with the oral cancer cells, multi-channel, rapid and quantitative detection of oral cancer cells was demonstrated.<sup>9</sup>

**cDNA microarray analysis** A study by Kondoh et al showed cDNA microarray analysis of OSCC and leukoplakias (LPs), showed that 11 gene predictors could best distinguish OSCCs from LPs (>97% accuracy), whereas a further 7 gene predictors could be used to distinguish higher grade (higher than moderate) from lower grade (lower than mild) dysplasias (>95% accuracy)<sup>10</sup>.

**Dielectrophoresis** It is a non invasive menthod to determine the conductivity, permittivity of cellular cytoplasm and membrane and other electrophysiological parameters and can be used as a potential tool for early detection of oral cancer<sup>11</sup>.

**Molecular Imaging in adjunct with CT,MRI and PET:**

Recent advances in molecular imaging techniques has build up the potential to enhance cancer diagnosis and staging by making characterized functional attributes of malignant cells visible. In recent days it has be shown in various studies that Molecular imaging applications can make properties of carcinogenesis visible at much earlier time points.<sup>12</sup>

**DISCUSSION**

Timely detection of oral cancers is as important factor as timely treatment of the same to achieve better prognosis and higher five year survival rate. The current standard for screening is visual examination, its correlation with deleterious habits or family history, histopathological study of the suspected lesion. Various imaging techniques are being used to justify the clinical evaluation and spread to regional lymph nodes. These techniques sometimes are not very successful in diagnosis potentially malignant lesions and oral cancers at an early stage, misleading to the situation. Delays in treatment initiation worsen up the prognosis and increase the risk and recurrence. Thus it is very important to have a timely diagnosis of such lesions as soon as they are reported. Early detection of oral cancers will not just help in beginning of treatment at an earlier stage but will also reduce the complications during and after the treatment and thus increasing over all five year survival rate. Science has advanced by many leaps in recent years leading to obvious advancements in field of medical diagnostics and imaging. FTIR spectroscopy, tissue fluorescence spectroscopy, adjunction of molecular imaging with Conventional diagnostic scans and Nanoroads are just to name a few of the recent advances in field of oral cancer diagnosis. Non invasive methods of cancer detection such as use of salivary markers, lugol's iodine and toludine blue and not just non invasive but also are cost effective and easily done task. Techniques of Molecular imaging give an early and clearly distinguished characterization between normal tissue, potentially malignant tissue and cancerous tissue at a very early stage. Tumor characterization without the need for invasive procedures such as biopsies or even surgery is considered another key feature molecular imaging adds to cancer diagnosis. Though these techniques are quite advanced and holds high specificity in regards to their results, none of the study in past have discussed in detail about the monitory issues related to same. Most of these techniques are in their trial phase and it will take a while for them to be available worldwide.

**Conclusion**

A lot is happening in the field of oncology, and a lot is yet to happen. We believe that availability of these advanced techniques in major cancer units around the world will aid in early detection of the disease and enhance the survival rate by leading to early treatment. By giving a comprehensive result these will also reduce the monitory burden and prevent unnecessary exposure to high radiations and multiple invasive biopsies.

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