



## SCREENING AIDS IN ORAL CANCER

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**ABSTRACT** Oral cancer is becoming more common around the world. Oral cancer patients have a low survival rate when compared to other types of cancer. This is mostly due to a delay in diagnosis, tumour spread, metastasis, and as a result, secondary tumours. Diagnosing oral precancer or oral cancer, especially in the early stages of the disease, is extremely difficult and crucial for the dental profession. Early detection and treatment planning for patients with oral cancer rely heavily on early screening and improved diagnostic tools. The importance of dental practitioners in the early identification of oral cancer is highlighted. As a result, every dentist should be up to date on recent breakthroughs in diagnostics in order to provide the best possible care to patients with malignant or pre-cancerous conditions.

**KEYWORDS** : screening aids, precancer, oral cancer, advances, diagnostic aids

Oral cancer is the third most frequent disease, affecting 20 people out of every 100,000 people and accounting for roughly 30% of all cancers. They can, however, be exceedingly dangerous if left untreated, even during the very early stages of the lesion. According to the National Cancer Institute's SEER programme, which gathers data on oral cancer, there has been little or no change in the diagnosis of oral malignancies at an early stage in the last twenty years.<sup>1</sup> Unfortunately, the majority of people are diagnosed when the disease has progressed to an advanced stage. As a result, early detection is critical in boosting public awareness and improving access to oral health care for all groups of people. There can absolutely be an increase in the survival rate by using modern diagnostic modalities that detect the disease in its early stages.<sup>2</sup>

#### Screening aids for oral cancer :

**VITAL STAINING** : Toluidine blue is used locally to aid in the detection of malignant changes and potential areas of high-grade dysplasia. When glycogen combines with iodine, it produces a brownish black stain, which is utilised to delimit the malignant change. The use of a combination of Lugol's iodine and toluidine blue in the diagnosis of high-risk patients and the selection of biopsy sites in wide-field malignancies prior to care is a valuable addition. The overall sensitivity of vital tissue staining for the detection of oral cancers is, with a specificity of 0.31 to 1.00.<sup>3</sup>

#### BRUSH BIOPSY :

The OralCDx Brush Test System was introduced in 1999 as a possible oral cancer diagnosis tool. The major target areas for brush biopsy were clinical lesions that would normally not be submitted to biopsy since the index of suspicion for malignancy was low based on clinical criteria. Oral CDx kits offered to investigators consist of an oral brush biopsy instrument, a precoded glass slide and matching coded test requisition form, an alcohol/ polyethylene glycol fixative pouch, and a preaddressed container to submit the contents. It can offer morphologic evidence of a range of benign oral processes, including candidiasis, herpes infection, pernicious anaemia, radiation damage, and pemphigus, in addition to precancer and cancer diagnosis. Oral CDx, on the other hand, is not a substitute for a biopsy.<sup>4</sup>

#### CHEMILUMINESCENCE :

The ViziLite plus uses a disposable chemiluminescent light packet, but

the MicroLux uses a battery-powered, reusable light source. Under blue-white illumination, normal epithelium appears light bluish, whereas aberrant epithelium appears notably white in appearance. The researchers used a single-use disposable chemiluminescent light stick that emits several wavelengths of light at wavelengths of 430, 540, and 580 nm. The normal epithelium absorbs light and appears dark, whereas precancerous states and lesions appear pale. In precancerous lesions and situations, the change in colour is linked to altered epithelial thickness and increased nuclear material and matrix of mitochondria, which reflects light more intensely.<sup>5</sup>

**OPTICAL COHERENCE TOMOGRAPHY** : Light is sent into tissues and reflected back in optical coherence tomography, similar to how sound waves are used in ultrasonography. As a result, half of the light beam is focused into the tissue being studied, while the other half is directed toward a reference mirror. The light is reflected off the mirror and tissue specimens, and the reflected beams are interfered with. Alternative light sources are being investigated in order to improve the image resolution. Advancement in this technology called the "Femtosecond transillumination tomography" has been shown to image up to a depth of 1.5 mm in experiments.<sup>6</sup>

**NARROW-EMISSION TISSUE FLUORESCENCE** : After stimulation of cellular fluorophores by a certain wavelength of light, autofluorescence of cellular fluorophores occurs. Visually Enhanced Lesion Scope comprises of light source and a component to assist in detailed examination or inspection. Normally, oral mucosal tissues emit a green-colored autofluorescence light, but abnormal oral mucosal lesions absorb the light and appear as darker patches. The VELscope was found to be useful in confirming oral premalignant lesions such as leukoplakia and erythroplakia in a recent study. The VELscope technology, on the other hand, shows promise because it is effective at detecting mucosal lesions and their borders that are hidden from intraoral clinical evaluation under white light.<sup>7</sup>

#### IDENTAFI 3000 :

Increased vascularization, a hallmark of cancer, causes spectroscopic differences between normal and potentially malignant tissue, which is the basis for the Identafi gadget, which is made by Star Dental Dental EZ, Lancaster. Based on the concepts of autofluorescence and

confocal microscopy, the Identafi 3000 examines the mouth with three wavelengths: white conventional light 405 nm for autofluorescence, and 445 nm green amber light for spectroscopic differences. In a recent study conducted by Schwarz et al., it was shown that Identafi 3000 has high sensitivity up to 82% and specificity up to 87%. Other advantages of the system include its small size and relatively higher access to all the tissue in the oral mucosa. Further studies yet need to be done to validate the clinical usefulness of this system.<sup>8</sup>

**IN VIVO CONFOCAL MICROSCOPY :** In vivo confocal microscopy is a new noninvasive imaging and diagnostic technology that allows researchers to examine surface microstructure in real time. It scans several points in parallel in section, volume, and sequence scan using a slit scanning microscope. It is unique in that it can image moderately opaque tissues and aid in the visualisation of dynamic processes such as inflammation and healing. As a result, it was first utilised in ophthalmology before being developed for use in the oral cavity. Pierce et al. employed a multimodal optical imaging system to evaluate 100 locations in 30 participants and presented their findings. In their experience, it successfully recognised 95% of anatomically normal areas and 98 percent of dysplastic and anaplastic lesions.<sup>9</sup>

**TISSUE FLUORESCENCE SPECTROSCOPY :** The absorption of photons by fluorophores occurs when oral cavity tissue is illuminated with UV-Visible light. It causes fluorophores to be excited, resulting in the emission of lower energy photons that are seen as fluorescence from the mucosal surface. The auto fluorescence spectroscopy system consists of a spectrograph that collects the continuums of reflected fluorescence from cellular structures and analyses the received information on a computer, as well as an optical fibre that is small and similarly generates wavelengths of variable excitations. According to a study, stimulation at 405 nm wavelength best distinguishes normal oral mucosa from oral premalignant lesions. The advantages of auto fluorescence can be overcome by using fluorescence-reflectance or dual digital systems, backscattered light analysis, and ultraviolet spectra.<sup>10</sup>

**ELASTOGRAPHY :** The hardness (elasticity) of lymph nodes is a key parameter for distinguishing between inflammatory and malignant enlargements. Elastography is a technique for determining cellular structural compliance. Compression of tissues causes displacement or strain in the tissue structure, and so the hardness of the tissue can be measured by measuring tissue strain. The pictures acquired by elastography are compared before and after cervical lymph node compression.<sup>11</sup>

**SURFACE ENHANCED RAMAN SPECTROSCOPY :** Because of the unique interaction of biological molecules with photons, Raman spectroscopy provides a realistic, high-resolution, and sensitive image of the molecular tissue structure. The spectral characteristics of lipids, nucleic acids, and proteins are used as accurate Raman biomarkers to distinguish between malignant and healthy oral mucosa. Raman spectroscopy provides information that is comparable to or even superior than known approaches in oral carcinogenesis. The downsides include the fact that it is non-imaging and random, as well as the fact that it necessitates expensive equipment, a lengthy process, a lack of spatial information, and complicated algorithms to distinguish various tissue classifications. These issues provide trials for their future use in therapeutic settings.<sup>12</sup>

**SALIVARY BIOMARKERS :** In the literature, more than a hundred possible oral cancer biomarkers in saliva have been described, based mostly on comparing the quantities recovered in oral cancer patients to the quantities found in people who serve as controls. Amylase, interleukin 8, tumour necrosis factor-, Statherin, CA 125, Endothelin-1, CD44, Catalase, Cyclin D1, CEA, Maspin, Lactate dehydrogenase, and Transferrin were among the salivary proteins examined. Salivary biomarkers are a promising non-invasive method, but there are significant obstacles to overcome. The lack of calibration for the salivary sample collection method, variability in processing and storing, extensive capriciousness concentrations of probable oral cancer biomarkers in saliva of both non-malignant individuals and oral cancer cases, and the need for additional validation are just a few of the challenges in their application.<sup>13</sup>

**CELL AND TISSUE MARKERS :** In addition to intra-oral clinical assessment and pathological examination, there are a variety of cell and tissue markers that could provide further information. Epithelial growth factor (EGF), Cyclins, AgNOR, bcl2, and telomerase were

employed as tumour growth markers. CD105 and Eph receptor tyrosine kinases (Ephs), vascular EGF, and four hypoxia biomarkers (GLUT-1, carbonic anhydrase IX, hypoxia inducible factor 1a, and erythropoietin receptor) were discovered to be biomarkers.<sup>14</sup>

**DNA PLOIDY ANALYSIS :** Recent research has suggested that DNA ploidy analysis could be used to predict the kind of premalignant lesions in the oral cavity. Aneuploidy (chromosomal imbalance) in dysplastic cells identified in premalignant lesions, as detected by high resolution flow cytometry, indicates a significant risk of mouth cancer transformation. DNA ploidy analysis compensates for intra- and inter-observer irregularities in the grading of dysplasia seen in premalignant lesions, and could potentially aid in directing the lesion's therapy, and likely indicate more aggressive treatment.<sup>15</sup>

**LAB ON A CHIP (LOC) :** Microfluidics technology is the adaption, miniaturisation, integration, and automation of analytical laboratory procedures into a single device or "chip," also known as lab-on-a-chip or micro-total-analysis systems. Microfluidics is frequently referred to as the chemical or biotechnology counterpart of the silicon integrated silicon chip, which has transformed electronics, computers, and communications. This microfluidic chip collects saliva samples, can be operated by anybody with little training, and can deliver a diagnosis in a rapid and automated manner. Membrane-associated cell proteins that are uniquely expressed on cell cancer cells will be used to detect oral precancer and cancer cells within the chip.<sup>16</sup>

**ARTIFICIAL INTELLIGENCE :** Artificial intelligence is a formidable technology to contend with because of its ability to handle vast amounts of data for decision-making in a quantified, repeatable, and customizable manner. Machine learning can help with cancer diagnosis decision-making, but there isn't enough evidence to use it in clinical practise now. Jeyaraj and Samuel Nadar developed a method for computer-aided diagnosis of oral cancer by employing a partitioned deep convolution neural network on hyperspectral photographs of patients. In a data set of 100 photos, they computed a sensitivity of 94% and a specificity of 91%, with 91.4% accuracy in distinguishing between malignant and benign lesions.<sup>17</sup>

## CONCLUSION :

Each of those diagnostic methods discloses its own uniqueness of technology in adjunctive roles of visual oral examination. Vital staining, oral cytology, and optical imaging diagnostics identify oral precancer or cancer lesions through direct optical visualization that are easy to use and create fast results. AI-based systems predict oral cancer via the training and analysis of large amounts of data, including images, clinicopathologic, and genetic data, whereas, LOC minimizes laboratory-scale biological molecule detection down to a small chip, both which may have a breakthrough in efficacy of oral cancer diagnosis.

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