Oral Brush Biopsy: Pros & Cons

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Introduction

Head and neck cancer is the 6th most common cancer worldwide[1]. In developing countries head & neck cancer is the most common form of cancer and represents a major health problem that will lead to the cause of death[2]. In Indian subcontinent, oral squamous cell carcinoma (OSCC) accounts for almost 40% of all cancers[3]. The main causative factor is the lack of improvement in prognosis over the last decades is the fact that a significant percentage of OSCC are not diagnosed or treated until they reach an advanced stage[4].

OSCC is proceeded by visible changes in the oral mucosa, such as: white plaque, redness, ulcer or exophytic lesion, with no other signs/symptoms. If OSCC is diagnosed and treated in this stage, it will be curable and inexpensive to treat with excellent treatment outcomes and survival[5]. 5-year survival is about 76% to 80% if diagnosis is performed in stage one and two. Late diagnosis in stage three and four can decrease this value to 41% and 9% respectively[6].

Despite advances in diagnostic procedures in medical practice, mortality of OSCC has remained very high in the past 40 years and a significant diagnostic delay (up to 8 months) has persisted over time[7].

Early detection of oral cancer is the most essential means of reducing the poor mortality from this disease[8]. If oral cancer is detected at its earliest stage, it can be readily cured; if the disease is detected at its precancerous stage, oral cancer is prevented[9]. Dentists who identify these types of early abnormalities in their patients can minimize the morbidity rate of the disease and its treatment, which are often associated with a severe loss of function, depression, disfigurement, and reduced quality of life[10].

Cytological study of oral cells is a relatively inexpensive, simple, non-invasive and risk-free technique that is well accepted by the patient. Oral epithelial cells can be obtained by a cyto brush that is easy to use in the oral cavity11.

List Of The Most Common Non-invasive Methods For The Diagnosis Of Oral Squamous Cell Carcinoma (oscc)[12]

1.	Toluidine Blue	Toluidine Blue Test
2.	Oral Brush Biopsy	1.Conventional Oral Brush Biopsy 2.Oral Brush Biopsy Assisted With Computer Assisted Analysis
3.	Saliva-based Oral Cancer Diagnosis	1.Genomic Substances 2.Transcriptomic Substances 3.Proteomic Substances
4.	Light-based Detection Systems	1.Chemiluminescence (microlux/dl, Vizilite Plus; Orascoptic-dk) 2.Tissue Fluorescence Imaging (velscope)
5.	Optical Biopsy:	1.Raman Spectroscopy 2.Tissue Fluorescence Spectroscopy 3.Elastic Scattering Spectroscopy 4.Differential Path-length Spectroscopy 5.Nuclear Magnetic Resonance Spectroscopy 6.Confocal Reflectance Microscopy (crm) 7.Optical Coherence Tomography Angle-resolved Low Coherence Interferometry (a/lci)
6.	Biomarkers:	1.Dna-analysis
7.	Laser Capture Microdissection	

Brush Biopsy

During the 1980s, for cervical smears in gynaecological lesions, a brush was developed and was later modified specially for oral smears too. This technique showed better cell spreading on the glass slides compared to smears obtained by using the conventional wooden spatula and also exhibited an improvement in the cellular morphology of the smears. The importance of oral brush biopsy was highlighted in a multi-centre study where about 5% of clinically benign-appearing oral mucosal lesions were sampled by applying this technique and later confirmed by using the scalpel biopsy to represent dysplastic epithelial changes or invasive cancer[10].

OralCDx (OralCDx Laboratories, Inc. Suffern, NY), the oral brush biopsy with computer aided analysis, is a diagnostic tool that identifies dysplasia in common oral spots that often have no suspicious clinical features. In comparison to exfoliative cytology, the brush biopsy technique collects cells from the full thickness of the oral epithelium. Oral brush biopsy is a chair-side, painless, easy to perform test that can be used to identify any suspicious lesion including common small white & red oral lesions to rule out dysplastic features. Since most oral lesions are benign in nature, most test results are likely to be benign. Almost 10% of all cases usually turn out to be abnormal. Based upon the results, the laboratory advises specific guidance on these abnormal cases sometimes recommending scalpel biopsy, observation or retesting [10].

	INDICATION13,14	CONTRAINDICATION
1.	White or red spots, chronic ulcerations mucosal lesions with an abnormal epithelial surface lesions	Lesions with intact normal epithelium
2.	Common, benign & small Abnormalities that have been routinely "watched" & not suspicious enough to warrant referral for biopsy	· Fibromas · Mucoceles · Hemangiomas · Submucosal masses · Pigmented lesion
3.	Harmless looking lesions.	Highly suspicious lesions (Immediate scalpel biopsy)
4.	Precancerous lesions	Lesions with obvious etiology: Herpes, Aphthous ulcers, Traumatic ulcers

The brush biopsy provides clinicians with a diagnostic-screening test similar to a Pap smear. The Pap smear is a procedure for the detection of cervical cancer in women. The brush biopsy is used only for patients with an oral, visible mucosal spot.[15]

Oralcdx Testing[16]:

1. Two Procedures

1. **Office Procedure** - OralCDx Brush Test.
2. **Laboratory Analysis** - Computer-assisted evaluation specifically designed for oral dysplasia.

2. OralCDx Test Kit: Components of kits

1. Oral Brush Test instrument (Figure 1)
2. Precoded glass slide & matching coded test requisition form
3. Alcohol/carbowax fixative pouch
4. Container for submitting the contents

OralCDx Brush Test

- Brush is sterile
- Two cutting surfaces
- Cytology instruments collect only superficial cells.
- Brush biopsy collects cells from all three epithelial layers: superficial, intermediate and basal.

3. Guidelines for Anesthesia

- Causes minimal or no bleeding or pain.
- Topical or local anesthesia is generally not required.
- For highly inflamed or ulcerated lesions, local or topical anesthesia may be used.

Topical anesthesia

- Gels, sprays and creams.
- Ointments should not be used.

4. Brush Biopsy Technique

- The flat surface should be used in most cases. (Figure 2)
- Apply firm pressure against the lesion – you should see a slight bend in the brush
- Rotate clockwise 10 times or more.

- Pink tissue or microbleeding indicates that the brush has penetrated to the basement membrane.
- If lesion bleeds, stop brushing and transfer material to slide.

For thick, white spots and for spots on the hard palate and gingiva

- Rotate very firmly and repeatedly over the centre and periphery of the lesion.
- May require 15 or 20 rotations.

For Ulcerations

- Only the periphery and not the centre of the ulcer.

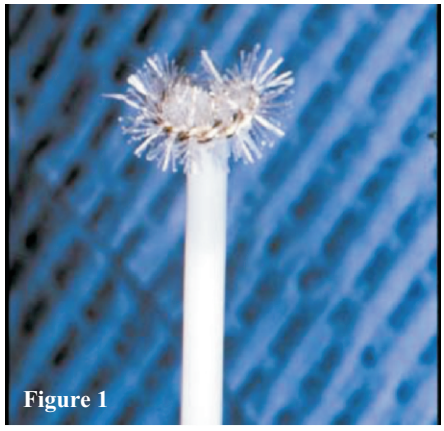
Figure 1


Figure 2

Figure 3

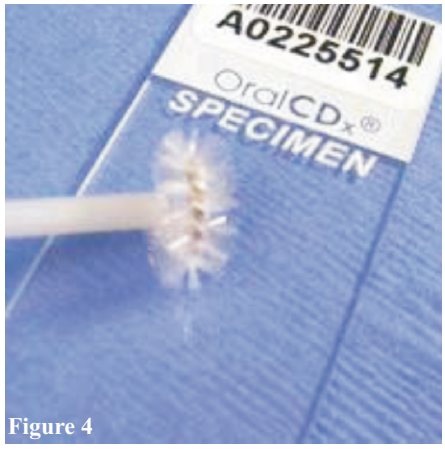

Figure 4

Figure 4


Figure 6

1. Oral Brush Test Instrument
2. Either the flat edge or the circular edge of the brush may be used to obtain a full-thickness epithelial biopsy.

3 & 4. Transfer cells onto the slide with the bar code facing up. It is important to rotate the brush over the entire length of the slide.

5. Immediately after the transfer, apply the fixative directly to the slide.
6. Computer assisted analysis of OralCDx Specimens

5. Transfer Cells

- Evenly spread the specimen over the entire slide —bar code facing up.
- Hold the slide up to a light – ensure the cellular material is visible on the slide. (Figure 3 & 4)

6. Apply Fixative

- By flooding slide with liquid (Figure 5)

7. Complete paperwork

8. Analysis of Oral CDx Specimens

Analysis of specimens is aided with a highly specialized which is neural network-based image processing system specifically designed to identify even the fewest oral precancerous and cancerous cells scattered among thousands of normal cells. (Figure 6)

9. OralCDx Interpretation

- OralCDx computer assists in the search for precancerous and cancerous cells.
- Pathologist utilizes both computer and standard microscopic evaluation.

10. Oral CDx Result[17,18]

1.	**"Inadequate"**	Re-test
2.	**"Negative"**	No cellular abnormalities
3.	**"Positive"**	Definitive cellular evidence of epithelial dysplasia or carcinoma
4.	**"Atypical"**	Abnormal cellular changes

How Does Oralcdx Help Prevent Oral Cancer?

- Every oral cancer started, years earlier, as a harmless appearing small white or red spot that is clinically identical to the ones you see almost daily.
- By testing every unexplained oral spot with the Brush Test you will identify, with high accuracy, which may contain unhealthy cells —years before they can penetrate the basement and cause any harm[14].

S. No.	ADVANTAGES19,20	DISADVANTAGES
1.	Provide earlier diagnosis of oral cancers & pre-malignantlesion.	Does not or cannot provide a definitive diagnosis
2.	In- office: Chair-side procedure.	It is not suitable to replace the conventional surgical biopsy methods.
3.	Easy to perform.	Detects only cellular atypia
4.	Minimally invasive procedure	Need to perform two procedure (Brush Test & Scalpel Biopsy)
5.	Less painful in comparison to scalpel biopsy.	Delay diagnosis
6.	No bleeding or Less bleeding in comparison to scalpel biopsy.	Adding time & cost

•Conclusion

Oral brush biopsy test can provide a better additional tool in the detection of questionable lesions by giving dentists an initial screening means before performing the scalpel/ incisional biopsy of lesions that had not clinically appeared to be oral cancer. It must be note down that cytology is an adjunct to, not an alternative for, a scalpel biopsy. Clinical examination and histopathological confirmation with biopsy will remain the gold standard for the identification and detection of oral cancer[21].

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