Educational Presentation to the ECCC

OralCDx Brush Biopsy - Technique and Indications

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Whatever happened to cervical cancer?

In 1950, cervical cancer was the leading cause of cancer death in American women.

Between 1955 and 1992, cervical cancer incidence fell from 1st to 14th place.
Cervical cancer was conquered because we found a way to tell which women had cervical dysplasia – years before cervical cancer could even start.

As in the cervix, if oral dysplasia is found and removed before the basement membrane is penetrated, then oral cancer can never get started.
How Your Dentist Can Prevent Oral Cancer From Ever Getting Started

Dysplasia

Years Later

Basement Membrane

Cancer

- It typically takes years before unhealthy cells found by OralCDx can penetrate the basement membrane and become harmful.
- During this time, the spot can be removed and the process is stopped.
The Dentist’s Dilemma

- **The Problem**
  
  - About 10% of adult patients have small oral spots
  - > 96% if these spots do not contain abnormal cells
  - Only laboratory testing can determine that a spot is not dysplastic.
  - Can’t subject 10% of all patients to a scalpel biopsy to find the small number of them that have a dysplastic spot.
The Dentist’s Dilemma

- The Result
  - Harmless appearing precancerous oral spots are often allowed to progress until they look “suspicious”
  - By that time they are typically oral cancers.
OralCDx BrushTest™
The Solution to the Dentist’s Dilemma

- A routine test of the small, harmless-appearing, white and red tissue spots that appear in about 10% of your patients

- Used to determine which 4% of these common spots contain unhealthy cells (dysplasia).

- OralCDx detects dysplasia long before it can penetrate the basement membrane and cause any harm – years before it can develop into an oral cancer
OralCDx BrushTest™
The Solution to the Dentist’s Dilemma

- OralCDx is not intended to test “suspicious” oral lesions. These should continue to be sent to the oral surgeon for a scalpel biopsy.

- OralCDx is intended to test “everyday” oral spots to detect the 4% of them which may contain still harmless dysplasia - years before a suspicious lesion can form.
Brush Biopsy Indications

- White or red spots, chronic ulcerations, mucosal lesions with an abnormal epithelial surface

- Common, small, benign-looking abnormalities that have been routinely “watched” and not suspicious enough to warrant referral for biopsy
Brush Biopsy Contraindications

- Lesions with intact normal epithelium
  - fibromas, mucoceles, hemangiomas, submucosal masses, pigmented lesions
  - highly suspicious lesions (immediate scalpel biopsy)
  - lesions with obvious etiology: herpes, aphthous ulcerations, trauma
## What to Expect in Your Practice

<table>
<thead>
<tr>
<th>Known benign entities</th>
<th>Harmless appearing, white or red spots of unknown origin</th>
<th>Highly suspicious lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>fibromas, mucoceles, linea alba, Fordyce granules, aphthous ulcers, traumatic ulcers, herpes labialis, amalgam tattoos</td>
<td></td>
</tr>
<tr>
<td>Frequency in average practice</td>
<td>Several times each day</td>
<td>Several times a week</td>
</tr>
<tr>
<td>Action</td>
<td>Observe or treat</td>
<td>BrushTest</td>
</tr>
</tbody>
</table>
“Small oral spots are very common. We see them in about 10% of our patients.”

“We BrushTest common oral spots because they sometimes contain unhealthy cells that may eventually become oral cancer if left untreated.”

“Even if a spot is found by the BrushTest to contain unhealthy cells that is nothing to worry about as it is typically still harmless. It can then be easily removed and we will have prevented a problem - years before it can even start.”
OralCDx Testing

Two Components

- Office Procedure - OralCDx BrushTest
- Laboratory Analysis - Computer-assisted inspection specifically designed for oral dysplasia.
The OralCDx Test Kit

Components of kits:

■ oral BrushTest instrument
■ precoded glass slide and matching coded test requisition form
■ alcohol/carbowax fixative pouch
■ container for submitting the contents
OralCDx BrushTest

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
EXFOLIATIVE CYTOLOGY
Only Surface Cells Captured

Broom sweep limited to superficial cells

SPECIMEN
Superficial
Intermediate
Basal
Exfoliative Oral Cytology

- Banoczy; *Int Dent J*: 1976
  - False negative rate for leukoplakia: 69%
- Folsom et al. 1972 *Oral Surgery*
  - False negative rate for oral cancer: 31%

Cytology is not an acceptable or reliable method of evaluating oral lesions for precancer and cancer
BRUSH BIOPSY
Complete Transepithelial Tissue Sample

OralCDx Brush Biopsy Instrument

SPECIMEN
Superficial
Intermediate
Basal
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 OK
    - ointments should not be used
Brush Biopsy Technique

Review

- The flat surface should be used in most cases.
- 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.
Tips for Performing a Brush Biopsy

- For **thick, white spots** and
- For spots on the **hard palate and gingiva**
  - rotate very firmly and repeatedly over the center and periphery of the lesion. May require 15 or 20 rotations
- For Ulcerations
  - sample only the periphery and not the center of the ulcer
The Brush Biopsy Technique

*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
The Brush Biopsy Technique

Apply Fixative
… by flooding slide with liquid

Complete paperwork
place slide and slide holder into mailer

Full instructions included in each OralCDx test kit
Analysis of OralCDx Specimens

Analysis is aided with a highly specialized neural network-based image processing system specifically designed to detect even the fewest oral precancerous and cancerous cells scattered among thousands of normal cells.
The OralCDx Computer

- Originally developed for missile defense
- Every brush biopsy specimen is analyzed for:
  - Abnormal cellular morphology
  - Signature spectral abnormality of the keratin protein
  - Cytometric evaluation of nuclear DNA content
OralCDx Interpretation

- OralCDx computer does not make the diagnosis
- OralCDx computer assists in the search for precancerous and cancerous cells
- Pathologist utilizes both computer and standard microscopic evaluation
OralCDx Laboratory selected images from OralCDx Display. Refer to full OralCDx test report form.
OralCDx Result

“Negative”

“Negative” - no cellular abnormalities

All OralCDx “negative” lesions require the same careful clinical follow-up as “negative” histologically sampled lesions

• Negative:

Follow-up information: Approximately 85% of OralCDx test results are “negative.” Lesions that change in appearance or that persist for more than six months after a negative report should be retested. Feel free to call the laboratory regarding your case.
OralCDx Result

“Positive”

“Positive” – definitive cellular evidence of epithelial dysplasia or carcinoma

- Almost every “positive” lesion will prove to be dysplasia or carcinoma

- Positive:
  
  Follow-up information: Approximately 1% of OralCDx tests are “positive” and these patients should have a scalpel biopsy. Please feel free to call the laboratory with any questions.

Scalpel biopsy to provide additional information regarding the nature and degree of the abnormality detected with OralCDx
OralCDx Result

“Atypical”

“Atypical” - abnormal cellular changes

- The probability that a patient with an “atypical” report has a precancer is ~ 40%

• Atypical:

Follow-up information: Approximately 15% of OralCDx test results are “atypical.” Of these, approximately 1/3 are found to be dysplastic on subsequent scalpel biopsy, and the remaining 2/3 are caused by other conditions such as inflammation. Depending on laboratory findings, it may be appropriate either to have the patient return in one month and repeat the brush biopsy or to have the patient evaluated for a scalpel biopsy. Please contact the laboratory for further guidance regarding your case.

The OralCDx laboratory can provide you with specific guidance on how to follow-up each “atypical” report.
Reports are faxed and mailed.

“positive” and “atypical” reports include images of abnormal cells found.
OralCDx BrushTest

- If you did not obtain a complete transepithelial sample – it is safe for you and the patient – the lab will notify you that the sample was “partial” and needs to be repeated.

- You will receive a “negative” report only if the sample was complete.
OralCDx MULTICENTER
U.S. TRIAL

- Participants: Oral Medicine, Oral Pathology and Oral Surgery Departments at 35 major U.S. Academic Dental Centers
- 945 patients enrolled
- Results were presented as the cover article of the Journal of the American Dental Association (JADA) October, 1999
DETECTING ORAL CANCER
Computer-assisted analysis of oral brush biopsy 1445

AMALGAM vs. RESIN-MODIFIED GLASS IONOMER CEMENT
Comparing their effectiveness in Class II restorations 1459

NIGHTGUARD VITAL BLEACHING
Assessing dentin color changes 1485
If an oral lesion would be found to be precancerous or cancerous using scalpel biopsy and histology, would it also be detected using CDx?

CDx correctly detected every lesion diagnosed as precancer or cancer using scalpel biopsy and histology (n=131)

Measured False Negative Rate = 0%

Statistical Sensitivity > 96%  p<.05
What is the probability that a lesion which is not dysplastic or cancerous will **not** have an abnormal OralCDx result?

- 100% (196/196) for “positive” CDx results
- 92.9% (182/196) for “atypical” CDx results

Statistical Specificity for a CDx “positive” > 97%, p < .05

Statistical Specificity for a CDx “atypical” > 90%, p < .05
OralCDx Positive Predictive Value

- Probability that a patient with an abnormal OralCDx result will be “positive” by scalpel biopsy

- The PPV of an abnormal OralCDx result is 2–16X higher than that of an abnormal mammogram or atypical Pap smear.
Scalpel Biopsy

Scalpel biopsy – invasive and associated with morbidity

- Reserved for highly suspicious lesions that may be cancer
- Infrequent: several times yearly

- Not for common, small, benign-looking lesions that may be dysplastic
- Frequent: several times weekly
OralCDx - One of the Most Accurate and Highly Predictive Tests in Medicine

Data from > 300,000 patients

SCALPEL BIOPSY

Positive Predictive Value (PPV)

The PPV of an atypical OralCDx ~ 40%
The PPV of an atypical Pap Smear is 5-20%
The PPV of an atypical Mammogram is 2.6-16%

100 Harmless appearing white or red spots which previously would not have been tested

14 atypical  5 Pos

14 atypical  10 Neg
The BrushTest in Practice

*JADA* Study: March, 2002

- 930 dentists and dental hygienists were examined
- 10% had a benign appearing oral lesion
- All lesions brush biopsied
- 3 lesions proven precancerous

*OralCDx* identified 3 precancers in dentists, preventing oral cancer from getting started
Adjunctive examination lights marketed as “aids to the oral cancer exam”

- Not “FDA approved” but “510K cleared” as “substantially equivalent to standard examination lights sold to dentists and physicians prior to 1976”
- Cannot be legally marketed as a “test” because the patient can have dysplasia and the light will not find it. Potential high false negative rate for early dysplasia.
- The BrushTest is the only non-invasive way to know that a common oral spot is not precancerous.
Toluidine Blue

For Carcinoma – High sensitivity
For Dysplasia – Very Low sensitivity
(high false negative rate )
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 BrushTest you will identify, with high accuracy, which may contain unhealthy cells – years before they can penetrate the basement and cause any harm.
How Your Dentist Can Prevent Oral Cancer From Ever Getting Started

- It typically takes years before unhealthy cells found by OralCDx can penetrate the basement membrane and become harmful.
- During this time the spot can be removed and the process is stopped.
OralCDx can be used to routinely test all unexplained spots to protect all of your patients against oral cancer
Reimbursement

The majority of both the dentist’s and the laboratory’s charges are covered by most dental and medical plans.

- Dentist’s fee for performing the test
  - Specific CDT Code is widely covered by dental $75-$125
  - Average fee for service range $120-175
  - Medicare > $120 – Important for nursing home practices
  - Dentist’s only cost is $10 for the OralCDx test kit.

- OralCDx laboratory Fee for analysis of the specimen
  - OralCDx lab bills the patient’s medical insurance $95
  - >97% of medical plans cover a portion of this fee.
Certification

- Patients who see the ADA advertising regarding the BrushTest contact OralCDx to learn which dentists use it routinely to protect their patients.

- Three course options
  - Lunch and Learn in your office
  - 15 minute conference call with dentists and staff
  - Free ADA CE [www.adaceonline.org](http://www.adaceonline.org)
OralCDx BrushTest Summary

- The tool to prevent oral cancer in all of your patients is painless, easy to use, and widely reimbursed.
- OralCDx has already been used to prevent thousands of oral cancers
- Free ADA Online Course: www.adaceonline.org
Detection of Dysplasia to Prevent Cancer

- Test For Dysplasia
  - Pap smear (1960’s)
  - Colonoscopy (1980’s)
  - Oral BrushTest (2000’s)

- Cancer Prevented
  - Cervical cancer
  - Colon cancer
  - Oral Cancer