

Accuracy of OralCDx

The accuracy of OralCDx was demonstrated in one of the largest dental studies ever conducted and performed at 35 academic universities in the United States, involving nearly 1000 patients (Statistical sensitivity > 96%, $p < .05$; statistical specificity of OralCDx “positive” > 97% and “atypia” > 90%, $p < .05$). Based upon this study, which was published as the cover story in JADA, OralCDx received the American Dental Association’s prestigious Seal of Acceptance.

In studies where brush biopsies and scalpel biopsies were performed concomitantly on the same lesion and by the same examiner, the high sensitivity and specificity of OralCDx, as determined in the US pivotal trial was replicated. An independent study performed in Europe validated the high accuracy of the computer-assisted oral brush biopsy. In the European study, scalpel biopsy results were compared with brush biopsy results that were obtained from lesions sampled concomitantly by the same examiner. The sensitivity for the brush biopsy was 92.3% (95% CI) and the specificity, 94.3% (95% CI).

The probability that a patient with an OralCDx “atypical” report has a precancerous or cancerous lesion, known as the positive predictive value, has been demonstrated in 5 independent clinical trials to be between 30%-44%. This is significantly higher than the positive predictive value for other cancer screening tests, such as the Pap smear and mammography.

The use of the oral brush biopsy as a highly accurate method of detecting precancers and cancers was incorporated into the 2006 National Cancer Institute’s Physician Data Query, better known as PDQ. (<http://www.cancer.gov/cancertopics/pdq/screening/oral/healthprofessional/allpages>). PDQ is the National Cancer Institute’s comprehensive cancer database and contains peer-reviewed summaries on many aspects related to cancer including screening and prevention. The PDQ cancer information summaries are peer reviewed and updated regularly by specialists, who review current literature from more than 70 biomedical journals, evaluate its relevance, and synthesize it into clear summaries. Summaries on screening/detection for many of the common cancers, including oral cancer, are available and include supporting references to current literature. Given the rigorous review process of PDQ involving specialists from all fields of medicine, we attribute the recognition of the brush biopsy into the oral cancer PDQ to the strength of the clinical studies demonstrating the benefits and accuracy of OralCDx.

Complete List of Publications

Sciubba JJ and the U.S. Collaborative OralCDx Study Group. *Improving detection of precancerous and cancerous oral lesions: Computer-assisted analysis of the oral brush biopsy*. U.S. Collaborative OralCDx Study Group. J Am Dent Assoc 1999;130:1445-1457.

- Cover story of JADA: pivotal multicenter study involving 35 academic centers.
- Phase 1: The sensitivity and specificity of OralCDx was determined by independently comparing results of brush biopsy with scalpel biopsy on the same lesion.
- Statistical sensitivity > 96%, $p < .05$, $n=131$; statistical specificity of OralCDx "positive" > 97% and "atypia" > 90%, $p < .05$, $n = 196$
- Phase 2: The added value of OralCDx as an adjunct to oral examination was determined by using the test on oral lesions that were judged clinically benign and not warranting a biopsy
- 29 of 646 oral lesions (4.5%) had a positive OralCDx result and all were ultimately confirmed by histology as dysplasia or carcinoma
- "OralCDx is a highly accurate method of detecting oral precancers and cancers. OralCDx is a valuable aid in confirming the benign nature of benign appearing oral lesions and more significantly, revealing those that are precancerous and cancerous when they are not clinically suspected."

Mehrotra R, Hullmann M, Smeets R, Reichert TE, Driemel O. Oral cytology revisited. *J Oral Pathol Med*. Feb 2009;38(2):161-166.

- "The improved accuracy of the OralCDx brush biopsy is due in part to the fact that it is the only instrument that was developed to sample the entire thickness of the epithelium – a transepithelial sample with cells from all layers are collected with this patented brush.
- "Furthermore, the analysis of the specimens is aided with a highly specialized neural network-based image processing system specifically designed to detect oral precancerous and cancerous cells, detecting as few as one or two abnormal cells scattered among tens of thousands of normal cells."
- "In every study in which the same lesion was simultaneously tested with both a brush and scalpel biopsy, OralCDx was shown to have a sensitivity and specificity well over 90%.
- "In addition, the positive and negative predictive values of OralCDx have been repeatedly shown in published studies to be substantially greater than other tests such as the Pap smear, mammogram, or PSA. Excellent positive predictive values of OralCDx was reported as 42% by Scheifele et al., 44% by Poate et al., and 38% by Svirsky et al., and 30% by Sciubba et al."

Scheifele C, Schmidt-Westhausen AM, Dietrich T, Reichart PA. *The sensitivity and specificity of the OralCDx technique: evaluation of 103 cases.* Oral Oncol. Sep 2004;40(8):824-828.

- European study determining sensitivity and specificity of OralCDx by comparing results of brush biopsy with scalpel biopsy on the same lesion.
- sensitivity 92.3% (95% CI); specificity: 94.3% (95% CI)
- "...these figures are in agreement with previously published data and support the use of OralCDx as a screening tool of oral lesions.."

Svirsky JA, Burns JC, Carpenter WM, et al. *Comparison of computer-assisted brush biopsy results with follow up scalpel biopsy and histology.* Gen Dent 2002;50:500.

- The positive predictive value of OralCDx was determined by 8 independent US oral pathology laboratories comparing brush biopsy results with subsequent follow-up scalpel biopsy results.
- The positive predictive value of an "atypical" OralCDx brush biopsy was 38%
- Only 1 confirmed false negative case was reported
- "...the value of the brush biopsy as a reliable method in testing harmless appearing lesions and as a means of ensuring that follow-up surgical biopsy is performed is unparalleled."
- "The improved accuracy is due to obtaining full transepithelial cellular samples and their evaluation with an image analysis system that was adapted specifically to detect oral epithelial abnormalities."
- "Delay in diagnosing oral cancers often is unavoidable due to many factors but the period of delay may be reduced in many cases with the brush biopsy tool, prompting earlier intervention and positively affecting treatment outcomes."

Kosicki DM, Riva C, Pajarola GF, Burkhardt A, Gratz K. OralCDx brush biopsy- A tool for early diagnosis of oral squamous cell carcinoma. Schweiz Monatsschr Zahnmed 2007;117: 222-7.

- The positive predictive value of "atypical" and "positive" OralCDx brush biopsies were determined in this Swedish study
- The positive predictive value (PPV) for the "atypical" CDx results was 42.9%, whereas the PPV for the "positive" CDx results was 100%.
- "The OralCDx brush biopsy is a minimally invasive screening method for surveillance of leukoplakia, erythroleukoplakia and early detection of innocuously appearing oral squamous cell carcinoma."

Christian DC. *Computer-assisted analysis of oral brush biopsies at an oral cancer screening program.* J Am Dent Assoc 2002;133:357-362.

- The added value of OralCDx as an adjunct to oral examination was demonstrated at a screening fair at 2 annual sessions of the American Dental Association
- 930 dentists and dental hygienists were screened and 89 (9.7%) had an oral lesion identified
- All lesions were evaluated by brush biopsy. 3 lesions, all clinically benign appearing, were OralCDx positive and subsequently proven by histology to be dysplasias.
- "This study confirms the data from other screening studies that have demonstrated that oral lesions are not rare, but are, in fact extremely common, even in people at low risk"
- "The identification of three innocuous-looking precancerous lesions in this low risk group of dentists and dental hygienists underscores the necessity of evaluating all oral lesions of unknown etiology."

Radensky PW, Archer JW, Cost-Effectiveness of Evaluating Benign-looking Lesions Detected During Routine Oral Examination. In Preparation

- "This study demonstrates that the oral brush biopsy is cost effective compared with watchful waiting for evaluating benign looking oral lesions."
- "Oral brush biopsy compares very favorably to these other tests by providing a gain in life expectancy with concomitant savings rather than increased costs per life year gained."
- "Performing oral brush biopsy rather than monitoring innocuous-appearing oral lesions may extend life expectancy and save health care costs. This strategy detects precancerous as well as cancerous lesions that otherwise look unsuspecting at a cost much lower than a number of well established screening tests for other forms of cancer."

Flaitz CM, Felefli S. *The Oral Brush Biopsy: It's as Easy as 1,2,3.* Texas Dental Journal 2000;117:20-24.

- "The oral brush biopsy technique, using computer-assisted analysis, is a highly accurate, user-friendly, and relatively noninvasive method for screening and monitoring oral lesions. When indicated, this procedure is a highly valuable tool in the continuing fight against oral cancer."

Zunt SL. *Transepithelial Brush Biopsy: an adjunctive diagnostic procedure.* J Indiana Dent Assoc 2001 Summer;80(2):6-8.

- "The oral brush biopsy overcomes obstacles that have impacted early oral cancer detection by eliminating guessing about which lesion requires surgical biopsy, reducing the tendency to delay referral of patients for scalpel biopsy, and reducing the hesitation of patients to comply with follow-up surgical biopsy."

Eisen D. *The oral brush biopsy: a new reason to screen every patient for oral cancer.* Gen Dent 2000;48:96-9.

- "Given the difficulty in clinically differentiating premalignant and malignant oral lesions from those that are benign, computer-assisted biopsy allows the dentist to test lesions that are encountered daily, thereby eliminating a barrier that has hindered the detection of early, curable oral cancers."

Svirsky JA, Burns JC, Page, DG, Abbey, LM. *Computer-assisted analysis of the oral brush biopsy.* Compendium 2001;22:99-106.

- "The use of the oral brush biopsy system for evaluating oral lesions that would have otherwise remained untested, has given the authors a greater appreciation of the effectiveness of this non-invasive diagnostic procedure."
- "By identifying potentially harmful oral lesions that would have ordinarily been "watched" or not referred for biopsy, early detection of cancers and their precursor lesions becomes possible. This is precisely why the computer-assisted brush biopsy analysis represents a breakthrough in oral diagnosis."

Tauberg JA *An oral surgeon's view of the computer-assisted oral brush biopsy.* Alpha Omegan 2002;95: 9-11.

- "OralCDx has revolutionized early diagnosis of the most life threatening of all dental-craniofacial conditions...oral cancer. Any dentist using this technology can have a significant impact on his or her patients' lives. Rarely is dentistry about life and death, but this is potentially life saving. I consider it an essential technology for every dental practice."

Drinnan, AJ. *Screening for Oral Cancer and Precancer- a valuable new technique.* General Dentistry 2000;48:656-660.

- "OralCDx provides a pain free, minimally invasive way for the practitioner to begin a diagnostic assessment of any suspicious epithelial oral lesion detected during an examination. It is especially invaluable for commonly occurring oral lesions that appear innocuous, those very same oral lesions that are encountered daily in your practice and until now have been ignored or infrequently subjected to testing."

Sciubba JJ. *Oral brush biopsy with computer-assisted analysis.*

eMedicine San Francisco, CA:eMedicine.com; Available at <http://www.emedicine.com/derm/topic701.htm>

- "The development of the brush biopsy (OralCDx) coupled with a computer-assisted method of analysis has brought accurate diagnosis, ease of performance, and patient acceptance into daily practice. In contrast to traditional exfoliative cytology, the brush biopsy, using a specially designed circular bristled brush, is able to access and sample all epithelial layers, including the basal cell layer and the most superficial aspects of the lamina propria. Thus, the cellular material obtained is a true representation of all epithelial layers"

Glazer H. *Detection of precancers and cancers of the oral cavity with computer assisted analysis of the brush biopsy.*

Independent Dentistry (London, UK): 2002;7 (3):85-89.

- "The oral brush biopsy is a minimally invasive, easily learned, patient accepted biopsy procedure that allows dentists to identify precancerous and early stage cancerous lesions. If routinely employed as a method of evaluating harmless-looking oral lesions that may in the past have been watched or ignored, dentists could detect early oral cancers that result in less radical treatment and improved survival."

Gurenlian JR. *The brush biopsy: A chairside technique for early detection of oral cancer*. Access 2003; September/October:32-36.

- "Most importantly, though, the OralCDx test provides a convenient method of testing an oral lesion, which is routinely encountered, yet never selected for traditional scalpel biopsy. These may include red or white lesions, for example, which appear too small or too harmless looking to refer for scalpel biopsy. Use of the OralCDx brush biopsy affords oral health care providers an opportunity to identify precancerous and cancerous lesions at early stages, when curative treatment can be provided."

Kerr AR, Cruz GD. *Oral cancer. Practical prevention and early detection for the dental team*. N Y State Dent J 2002 ;68:44-54.

- "The OralCDx brush biopsy is simple, painless and highly accurate.... This technique can and should be carried out in every dental office."

Laskin DM. *Early diagnosis of squamous carcinoma*. J Oral Maxillofacial Surg 2003;61:851-2.

- "Use of the brush biopsy for small, nonsuspicious-looking areas brings new meaning to what was previously considered 'early diagnosis'. Combining this procedure with careful clinical examination should go a long way to toward producing a significant improvement in the cure rate for oral cancer."

Stahl S, Meskin LH, Brown LJ. *The American Dental Association's oral cancer campaign: the impact on consumers and dentists*. J Am Dent Assoc 2004;13:1261-1267.

- "As the brush biopsy is indicated to test lesions that do not appear to be suspicious and would not have been referred for scalpel biopsy, identifying unsuspected cancers in their early stages can significantly improve survival of patients with these types of lesions. The findings of our survey demonstrate that general dentists are evaluating more small lesions utilizing the brush biopsy and referring more patients with oral lesions (those with abnormal brush biopsy results) to the oral surgeon. Prior to the advent of the brush biopsy, many of these small lesions were watched repeatedly until they changed to a more serious and advanced stage. From our survey, it is clear that the brush biopsy is having a positive impact on dentists who utilize it to evaluate small lesions, and such a change can only result in the detection of a greater number of early cancers."

Oral Cancer. The American Association of Oral and Maxillofacial Surgeons (AAOMS) Surgical Update. 2003; Volume 18:1-7.

- "The brush biopsy is an office procedure that may be performed without local anesthesia. A complete transepithelial sample is scanned by a computer system, with particular attention to abnormal cellular morphology and abnormal keratinization, features that characterize dysplasia and carcinoma of the oral epithelium. 'Brush biopsy' may be used as a screening tool."

American Dental Association: Dental Product Spotlight.

Journal of the American Dental Association 2001;132: 215.

- "OralCDx can help determine the significance of an oral lesion and help detect innocuous-appearing oral cancers at an early, curable stage. Highly accurate method of helping the early detection of precancerous and cancerous oral lesions."

Glazer H. Oral Cancer: "Be sure or get sued".

AGD Impact 2002;30:16.

- "With the widespread acceptance of the brush biopsy by general dentists nationwide, "failure to diagnose" and "failure to biopsy" oral lesions, which may represent oral cancer, should never be allegations that dentists have to defend. Since the brush biopsy is a not a difficult procedure to perform, requires no anesthesia, and causes minimal or no bleeding or pain, and carries the ADA Seal of Acceptance, the failure to evaluate oral lesions that may be precancerous or cancerous, even when you do not suspect them of being so, is inexcusable, and makes you liable!"

Moore L. Advancing technologies for oral cancer screening.

J California Dental Hygienists' Association 2003;18:18-24.

- "OralCDx is an accurate method of detecting oral precancerous and cancerous lesions. Specifically, the test is indicated for oral lesions with an epithelial abnormality, which appear harmless and would not have been evaluated by scalpel biopsy. It is an effective diagnostic tool for those lesions which otherwise would have been watched."

Curry JT. *Benefits of the brush biopsy.*
J Oral Maxillofacial Surg 2003;61:1506

- "Since many potentially dangerous lesions are being detected among lesions that would not have been evaluated, I think the benefit of the brush biopsy cannot be overstated. Dentists now have the opportunity to evaluate harmless-appearing lesions other than by watchful observation and, with the assistance of the OMS, can uncover unsuspected precancers and cancers in early stages."

Edwards J. *New test aids in early diagnosis.*
Access 2000;14:25.

- "The test, in conjunction with a thorough oral cavity cancer screening examination, can have the impact that mammography has had on breast cancer and that Pap smears have had on cervical cancer."

Leonard, M. *New Techniques for Diagnosing Oral Cancer.*
Dental Economics 2000;June:126-131.

- ".. this technology can enhance, not only the thoroughness of one's oral exam, but also one's diagnostic skills and clinical acumen. When one examines either a new patient or a patient at a six monthly recall, areas that previously were put "on hold" can now be brush biopsied in minutes. Areas that a patient has noticed – though it's not often the case – can be brush biopsied at a moment's notice.