

**AADC Positions Committee \***  
**FINAL Position Statement**  
**Oral Cancer Screening-Adjunctive Diagnostic Aids**  
**September 24, 2008**

**Introduction**

Oral cancer has emerged as a significant health concern. Current statistics show that approx. 34,000 people will be diagnosed with oral cancer this year and upwards of 8,000 will die from the disease. Oral cancer has typically been diagnosed primarily in older patients (40+ years old) or patients with known risk factors including tobacco and alcohol use. There is some evidence that these trends may be changing and a larger cross section of the population may be at risk. The link between certain strains of human papilloma virus and oral cancer has increased the risk of disease in the 20-40 year old demographic. Of even greater concern is the fact that 25% of all oral cancer cases occur in patients with no known risk factors. This underscores the need for dentists to conduct routine oral cancer screenings and consider adoption of new and proven screening tools that may serve to advance diagnostic outcomes for specific patient populations.

**Background**

Public awareness regarding the risk factors and signs and symptoms of oral cancer has historically been low. However, public service campaigns have been launched over the past couple of years by the ADA, state dental societies, and other organizations in an effort to educate the general public about oral cancer and the importance of receiving oral cancer screenings from their dentists in conjunction with routine preventive and diagnostic visits.

When oral cancer screenings are conducted, the screenings have historically been limited to visual and tactile examination of the oral soft tissue under incandescent lighting. New technology has emerged, including soft tissue chemiluminescence and soft tissue fluorescence, which reportedly provides dentists with additional diagnostic testing modalities to supplement the standard visual and tactile soft tissue examinations. Developers of these diagnostic aids assert that the tests are able to identify both malignant and pre-malignant lesions in the earliest stages of development.

The basic concept behind chemiluminescence and fluorescence is based on evidence that changes in the oral mucosa including inflammation, regeneration, dysplasia, pre-malignancy, and malignant transformation will demonstrate different patterns of light absorption and reflection when compared to normal tissue. Tissue chemiluminescence involves a non-invasive, one or two-step procedure that utilizes an initial rinse with an acetic acid solution. The acetic acid rinse serves to identify abnormal epithelial cells. Upon visual examination of the mucosa with application of a blue-white light, abnormal

and normal mucosal tissue will demonstrate distinct patterns of light reflectance. Normal tissue exhibits a light blue appearance while abnormal tissue exhibits a distinct white appearance (known as “acetowhite”). Suspicious acetowhite areas can be further evaluated with an application of a toluidine blue stain. Toluidine blue stain selectively binds to the DNA of cells that may be damaged or undergoing increased metabolic activity. Abnormal tissue stained with toluidine blue will exhibit a dark blue appearance. Tissue fluorescence is based on the principle that the cells of the oral mucosa will naturally fluoresce upon application of blue light due to the presence of fluorophores within the cells. The test is a non-invasive one-step procedure. Upon application of the light, normal mucosal tissue exhibits a pale green appearance while abnormal tissue exhibits a darker or black appearance due to the loss of natural fluorescence.

Regardless of the oral cancer screening methodology employed, any suspicious sites should be biopsied for definitive histopathological analysis. The brush biopsy has emerged as a useful adjunct test for in-office use by dentists. The brush biopsy is a non-surgical, minimally invasive procedure that uses a small brush to collect a transepithelial cell sample at the suspicious site. The sample is sent to a lab where, through computer-aided microscopic analysis, the cells are classified as negative, positive, or atypical. Despite the utility of the brush biopsy, the scalpel or punch biopsy remains the gold standard for histopathological tissue analysis. When cells have been identified as positive or atypical by the brush biopsy, a follow-up scalpel or punch biopsy should subsequently be conducted on the patient in order to determine a definitive histopathological profile of the tissue.

Oral cancer diagnosed at the earliest stages of the disease result in significantly higher survival rates and significantly lowers morbidity when compared to late stage diagnosis. Medical costs for treating a patient with advanced oral cancer have been estimated to be approx. \$200,000. Improved methods for oral cancer screening would enhance a healthcare professional's ability to diagnose oral cancer in its early stages and allow for early treatment interventions. This would serve to improve the long-term prognosis for the patient and reduce potential healthcare costs.

The objective of this position paper is to evaluate the outcomes of the available scientific evidence related to oral cancer adjunctive diagnostic aids and determine if the clinical studies support the diagnostic value of these aids above and beyond traditional visual and tactile screening. Recognizing that oral cancer is a serious healthcare problem with the potential to significantly impact patients, providers and payers, the science should confirm that these diagnostic aids truly add value and can contribute to improving patient health outcomes.

### **Summary of Evidence**

The ongoing desire by the healthcare industry to provide methods of cancer detection in both a consistent and highly correlated statistical reliability has been a long term ongoing enterprise. The relevance to the oral clinical setting has, within the last decade, taken on

additional importance as a result of the increased recognition of the overall health benefit of oral cancer detection.

While the adjunctive diagnostic aids reviewed here vary, the goals of the designer's seem to have common elements of simplicity of testing and reasonable economic cost.

Highlights of the review of the testing methods included:

- Procedures were designed to be easy to implement in a clinical office setting for use by general practitioners.
- Procedures had a variance in approaches as to how to detect the predisposition and presence of oral lesions as well as conditions under which the procedure would be most appropriate to use.
- For the most part, all the procedures relied on verification through excisional biopsy as the most valid means of verification.
- The procedures were non-invasive (the brush biopsy is minimally invasive).
- Procedures attempted to be derived in a cost environment that allows for both minimal cost and hence widespread application.

Subsequent review of the literature has yielded an array of results which can be characterized as inconclusive. There was neither a high correlation of testing validity as a predictor of oral cancer or definitive economic impact relative to medical savings downstream as a result of the widespread incorporation of such tests. It was this lack of high correlation that challenged the Committee relative to coming up with conclusive findings when reviewing the associated literature. Some of the highlights of the literature and observations of Committee members are presented below.

- While reducing medical costs through early detection is a worthwhile endeavor and seems to imply economic benefits, the cost of these oral cancer screening exams should also be considered in their relative ability to consistently predict the presence of an oral lesion. For example, tissue chemiluminescence is reported to be relatively expensive with the cost per unit of one of the best known brands in the range of \$24 to \$28. It should also be noted that each test can be used once per patient. Proponents of these screening procedures claim that early detection will decrease costs over the long term since more advanced and more expensive surgical procedures can be avoided. However, there are no long term studies to support any long term cost reduction. Further; there are few if any studies that provide the ratio of early oral cancer detections per tests provided, particularly those detected that would not have been detected by traditional careful visual examinations.
- The value of these methodologies will be impacted by the consistent application of these tests throughout a specified patient base. As such, there is a large

variance in general guidelines for testing such that the final use of these tests will probably be subject to the individual dentist's determination of who should be tested. So, other than large scale controlled testing, actual real world impacts will vary greatly.

- There are also concerns at the limited or no long term tracking of both false positives and dysplastic lesions, to determine if and when they evolve into a true oral cancer. This begs the question, what will be the additional cost of biopsies to differentiate the true positives from the false positives. The emotional impact of such processes should not be understated.
- Another question unanswered by current research is how many diagnosed cases of late stage oral cancer undiscovered by routine visual examination would have been discovered at an earlier state if adjunct procedures were used. This is where the value of these procedures should be demonstrated. As such, there is no clear cut inherent value associated with any of these tests.
- There is mixed evidence on the efficacy of toluidine blue as an adjunctive diagnostic aid. While there is evidence suggesting that toluidine blue is a useful diagnostic adjunct in high risk patients or to identify suspicious lesions, there is insufficient evidence supporting its value in the screening of apparently healthy individuals. Additionally, some studies have found that toluidine blue staining of an identified lesion reduces the number of false positive biopsies performed without any increase in the false negative rate
- Tissue chemiluminescence has been reported to be nonspecific and may prompt the performance of unneeded biopsies. Examination of the oral tissue with tissue chemiluminescence illumination did not change the provisional diagnosis, nor alter the biopsy site. Tissue chemiluminescence does not discriminate between keratotic, inflammatory, malignant or potentially malignant oral mucosal white lesions and thus, a high index of suspicion, expert clinical judgment, and scalpel biopsy are still essential for proper patient care. Additionally, although using an acetic acid rinse may have some benefit in making mucosal changes more visible, there appears to be no added benefit from using a chemiluminescent light rather than incandescent light for subsequent oral examination.
- Some studies have reported that tissue fluorescence is useful in assessing lesion margins in patients with pre-malignant lesions and may be beneficial for surgical planning and management. However, there are currently no studies available assessing the value of tissue fluorescence as a diagnostic adjunct in low risk patient populations or in patients seen by primary care providers. It is also important to note that cells of the oral mucosa exhibit variability in the amount of fluorescence and loss of fluorescence may be seen in otherwise benign lesions.

- There is insufficient evidence to suggest that adjunctive methods of oral cancer screening including toluidine blue, soft tissue fluorescence, or brush biopsy, are either beneficial or harmful. Future high quality studies to assess the efficacy and effectiveness of these tools are needed. In addition, studies to elucidate the natural history of oral cancer, prevention methods and the effectiveness of opportunistic screening in high risk groups are needed.
- The ADA Council on Scientific Affairs has also given consideration to the value of certain oral cancer adjunctive diagnostic aids. In its review of an application for the ADA Seal of Acceptance for a tissue chemiluminescence system, the Council denied the Seal of Acceptance for the product based on the weakness of the submitted study data.

### **Position Statement**

Based on the available evidence, it is the recommendation of the Committee, that, given the current state of oral cancer screening:

- There is not at this time, sufficient evidence to provide for definitive health and economic impact through the large scale application of any of the adjunctive diagnostic aids reviewed. The use of such aids will benefit certain individuals under certain conditions, but the degree of variance, false positives and other environmental or genetic dispositions make prediction of who these individuals would be very difficult at this time. Therefore, the Committee believes that adjunctive aids be primarily utilized for oral cancer at-risk patient populations and cannot recommend any widespread use of any of the aids reviewed
- Clearly, the potential evolution, refinement, and greater longitudinal research of these aids will hopefully provide a greater and more consistent efficacy. The Committee recommends that when more relevant and statistically useful information is available, the current state of oral cancer screening aids be re-evaluated.
- The Committee clearly recognizes the tremendous value imparted through increased awareness through both proactive ADA actions as well as increased patient awareness engendered by the dental community and supports continued promotion of such programs to increase patient awareness. The Committee would recommend that the dental community ensure that incorporation of any of the aids in their diagnostic protocols be accompanied by patient education as to the inherent potential benefits and limitations of any of the aids reviewed. New technology and even its attendant marketing has clearly made a positive impact on the field of dentistry by encouraging clinicians to more routinely perform thorough oral cancer exams
- Finally, the Committee recommends that the classic visual and tactile methods used in current oral cancer screening be a routine part of any clinical exam.

## Next Steps

- Presentation of the position paper to the AADC Board of Directors for review, comments and recommendations, and final approval
- Share with key stakeholders as identified by the AADC Board
- Share with AADC members and other interested parties through posting on the AADC website and publication in the *Beacon*
- Continued surveillance of the scientific literature to evaluate the evolution of adjunctive diagnostic aids and the outcomes of future clinical studies

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**\* AADC Positions Committee**

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