Assessment of oral mucosal lesions with autofluorescence imaging and reflectance spectroscopy

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ABSTRACT

Background. The aim of this prospective study was to evaluate the efficacy of a new form of autofluorescence imaging and tissue reflectance spectroscopy (Identafi, DentalEZ) in examining patients with oral mucosal lesions.

Methods. The authors examined 88 patients with 231 oral mucosal lesions by conventional oral examination (COE) using white-light illumination and ×2.5 magnification loupes, followed by examination using Identafi. The authors noted fluorescence visualization loss, the presence of blanching, and diffuseness of vasculature. They performed incisional biopsies to provide definitive histopathologic diagnosis.

Results. Identafi's white light produced lesion visibility and border distinctness equivalent to COE. Identafi's violet light displayed a sensitivity of 12.5% and specificity of 85.4% for detection of oral epithelial dysplasia (OED). The authors noted visible vasculature using the green-amber light in 40.9% of lesions.

Conclusions. Identafi's intraoral white light provided detailed visualization of oral mucosal lesions comparable with examination using an extraoral white-light source with magnification. A high level of clinical experience is required to interpret the results of autofluorescence examination as the violet light displayed low sensitivity for detection of OED. The green-amber light provided additional clinical information in relation to underlying vasculature and inflammation of lesions.

Practical Implications. Examination using Identafi can provide clinicians with more clinical data than a standard COE with yellow incandescent light, but the clinical and optical findings should be interpreted as a whole and not in isolation. Clinicians should use the light features of Identafi in a sequential and differential manner.

Key Words. Oral cancer; oral leukoplakia; tissue fluorescence; oral diagnosis.

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Oral cancer is the sixth most common malignancy globally, with an estimated 263,900 new cases and 128,000 deaths in 2008 alone.[1-3] Oral squamous cell carcinoma (OSCC) affects the oral mucosal lining of the oral cavity and accounts for 90% of oral cavity cancers.[1,2]

Risk factors for the development of OSCC include tobacco use, excessive alcohol consumption, and betel quid use.[3,4] Infection of the oral cavity with human papillomavirus also has been implicated as a contributory factor in patients who do not have traditional risk factors, although this association appears to occur in only a small subset of patients with OSCC.[5,6]

Despite advances in oncologic therapy, global 5-year survival rates for OSCC have remained at approximately 50% over the past 3 decades.[7,8] This rate is attributed predominantly to delayed diagnosis, as there are vastly improved 5-year survival rates associated with stage I and II cases in which the cancer is a localized disease process.[4] Despite the importance of tumor staging as a prognostic determinant of survival outcomes, clinicians still are diagnosing 60% of OSCCs in patients who are at stages III and IV, attributing to the low survival rate.[4,9,10]

OSCC frequently is preceded by clinically identifiable oral potentially malignant lesions (OPML) that correspond with an increased risk of experiencing cancerous change.[11-14] Early detection of OPML is the most effective method for improving patient survival and decreasing patient mortality; however, early detection is hindered by the clinical subtlety associated with such lesions.[13,15,16]

The standard for the detection of oral mucosal lesions is a conventional oral examination (COE) involving visual inspection and digital palpation of the oral cavity

using incandescent yellow light in most circumstances. However, this technique, when conducted by general practitioners, is associated with poor sensitivity for the detection of precancerous lesions and makes it difficult for the clinician to differentiate between progressive and nonprogressive lesions.[9,16-20] These limitations have driven the development of new technologies designed to aid clinicians in detecting oral mucosal lesions with a high level of sensitivity and specificity.[21] Manufacturers have developed several commercially available adjunctive examination devices to aid clinicians in detecting and examining oral mucosal lesions and to identify whether such lesions harbor oral epithelial dysplasia (OED) and are therefore at increased risk of developing into OSCC. The aim of this prospective study was to evaluate the efficacy of a new form of autofluorescence imaging and tissue reflectance spectroscopy (Identafi, DentalEZ) in examining patients with such oral mucosal lesions.

Identafi is an intraoral, multispectral screening device featuring 3 lights of different wavelengths that are used sequentially to examine oral tissues.[22] In addition to a light-emitting diode (LED) white light, the device also includes violet (405 nanometer) and green-amber (545 nm) lights to induce tissue fluorescence and reflectance spectroscopy, respectively. White light provides superior visualization of oral mucosal lesions compared with incandescent light, and as such, it has been included as the first light feature.[23] Identafi's violet light is known to excite blue fluorescence in normal mucosa, whereas abnormal tissue appears darker owing to fluorescence visualization loss (FVL).[22] Identafi is also the first commercially available handheld, intraoral device to include assessment of tissue reflectance spectroscopy in determining the status of suspected lesions.[21] The morphology of tissue vasculature can aid clinicians in evaluating oral mucosal lesions, and the green-amber light delineates these underlying vessels.[24-26] The investigators of previous studies that focused on Identafi did not compare the efficacy of the device with COE and failed to evaluate the clinical utility of the intraoral white light in comparison with an extraoral or incandescent light source.[21]

With this study, we aimed to be the first investigators to evaluate the efficacy of an enhanced Identafi model in examining and monitoring patients with oral mucosal lesions in a specialist setting. A secondary purpose of our study was to offer commentary on the utility of the white and green-amber light features.

METHODS

We conducted this study in accordance with human ethics guidelines approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC/10/QRBW/336), and we designed the study in accordance with the Standards for Reporting of Diagnostic Accuracy Studies guidelines.[27] We obtained written informed consent from each participant of the study.

Over a 5-month period from March through July 2013, we invited 288 new and existing patients[23,28,29] to participate in the study at a single-site oral medicine and pathology specialist referral practice in Brisbane, Queensland, Australia, that was serviced by a single oral medicine specialist (C.S.F.) who conducted the initial and review clinical examinations for all patients.[30] The only criterion for inclusion was the presence of a white, red, or mixed red-white lesion. We recorded patients' age, sex, smoking history, alcohol consumption habits, and use of mouthwash with corresponding alcohol content on the basis of study results we have previously published.[23,28,29] We performed COE using ×2.5 magnification loupes (HiRes 2 [2.5×], Orascoptic) and a white LED headlight (Discovery, Orascoptic). We recorded the location, size, color, ease of visibility, and border distinctness for each lesion. We ranked the ease of visibility as either excellent (that is, a lesion that was prominent and clearly visible) or poor (that is, a lesion that was faint and less apparent clinically).

We also recorded a provisional clinical diagnosis for all lesions in accordance with our previously published studies.[23,28,29] We grouped lesions into the following 4 categories described previously[29]: homogeneous leukoplakia (that is, a nonwipeable homogeneous white patch with no apparent etiology); nonhomogeneous leukoplakia or clinically suspicious for malignancy (that is, mixed red-white or mixed red-white ulcerated lesions with a high index of suspicion for OED or OSCC); lesions with lichenoid features suggestive of oral lichen planus, oral lichenoid reaction, or both; and other types of lesions (such as vascular or pigmented lesions). The nonhomogeneous category included lesions that were heterogeneous in both color and texture.

We then conducted examinations using Identafi's 3 light features in sequence. We first used Identafi's white light without magnification, and we repeated all measurements taken during the COE. Then we dimmed the room and operatory lights and repeated all previous measurements using Identafi's violet light.

Our assessment of autofluorescence included classifying the degree of autofluorescence of each lesion by using following terms: gain, no loss, or loss of autofluorescence. We considered lesions that displayed FVL to be positive and lesions that displayed no loss or fluorescence visualization retained (FVR) (also known as

ABBREVIATION KEY. **COE:** Conventional oral examination. **FN:** False negative. **FP:** False positive. **FVI:** Fluorescence visualization increased. **FVL:** Fluorescence visualization loss. **FVR:** Fluorescence visualization retained. **ID:** Identification. **LED:** Light-emitting diode. **NA:** Not applicable. **NPV:** Negative predictive value. **OED:** Oral epithelial dysplasia. **OPML:** Oral potentially malignant lesions. **OSCC:** Oral squamous cell carcinoma. **PPV:** Positive predictive value. **TN:** True negative. **TP:** True positive.