Fluorescence Visualization Devices in General Dentistry: Seeing the Big Picture

David C. Morgan, PhD, Chief Science Officer, LED Dental Inc.

Dental professionals have been traditionally limited to the use of incandescent light for the visual inspection of the oral cavity. Direct visualization of reflected white light from mucosal surfaces can enable the detection of gross tissue abnormalities, but may fail to identify some early disease processes (such as dysplasia) that have not yet caused changes easily observed using incandescent light.

The limitations of white light have stimulated the search for alternative modalities, and in 2006, after extensive research, the VELscope system was approved in Canada and cleared by the FDA in the United States. Like subsequent entries in its category, such as the Identifi 3000, and the Sapphire Plus Lesion Detection, the VELscope is a non-invasive, handheld device that allows the direct visualization of oral-cavity fluorescence. There are currently two approved indications for the use of oral fluorescence visualization devices: to help clinicians detect cancerous and precancerous lesions and other lesions that might not be apparent to the naked eye, and to help specialists determine appropriate surgical margins.

The VELscope induces natural tissue fluorescence by illuminating the oral cavity with a bright blue light. The resulting tissue fluorescence is significantly dimmer than the blue excitation light reflected from the tissue, but can be directly visualized by looking through the device's handpiece, which blocks reflected light and optimizes contrast with filters situated along the viewing path.

Mucosal abnormalities often present with abnormal fluorescence patterns that can aid the user in detecting unhealthy tissue. Decreased tissue fluorescence resulting in abnormal fluorescence patterns arises from a variety of causes[1], including:

- Increases in metabolic activity in the epithelium.

- Breakdown of the fluorescent collagen cross-links in the connective tissue layer beneath the basement membrane.

- Increase in tissue blood content, either from inflammation or angiogenesis (hemoglobin strongly absorbs fluorescence excitation [blue] and emission light [green]).

- Presence of pigments (e.g. melanin or amalgam particles) which absorb light.

Fluorescence visualization devices are particularly sensitive to dysplasia and cancer, disease processes which often involve the first three of the mechanisms bulleted above. Inflammation, on the other hand, is a common occurrence in the oral cavity and also presents as a strong loss of fluorescence, as will certain normal tissues, usually because of their high vascularity or associated blood content. Clinicians utilizing fluorescence devices should familiarize themselves with the normal appearance and patterns of oral cavity fluorescence. This will better equip them to recognize abnormal patterns when they present.

By definition, the use of an adjunctive device is subordinate to a larger diagnostic picture and should not be thought of as a diagnostic test with a definitive "yes/no" or "positive/negative" answer. To properly understand the significance of the fluorescence examination, it must be considered together with the head and neck visual and tactile exam — which itself is embedded within a larger diagnostic process that includes health history, patient interview, and biopsy when required. A particular fluorescence pattern or loss of fluorescence can mean different things in different clinical contexts. Fluorescence visualization never replaces the clinical judgment of the clinician nor overrules areas of concern discovered by means of the traditional examination. The value of fluorescence visualization lies in the fact that it is based on a different type of interaction with tissue than conventional reflectance of white light, and can therefore show the clinician areas of concern that may have been missed during the white light exam. This can lead to the early discovery of lesions, with consequent benefits: enhanced quality of care provision for the clinician; more effective, less invasive therapeutic intervention for the patient; potential improvement of the patient's quality of life.

Over the past six years, considerable research has attempted to evaluate the use of fluorescence visualization (predominantly focused on the VELscope system) as an aid for the general dentist and specialist.[1-18] In addition, some review articles have attempted to evaluate the general benefits of oral cancer screening, and of adjunctive aids such as VELscope.[19-21] This work has encompassed a broad spectrum of applications and methodologies; in particular, there has been excellent research devoted to surgical applications. Some of the research directed towards general use by dentists, however, adopts a narrow vision of the utility of the technology, and often fails to evaluate the device according to its stated indications for use. In particular, many authors compare the use of fluorescence visualization to a head and neck exam as a standalone diagnostic procedure for oral cancer, instead of evaluating the *added value* of using fluorescence visualization *in combination* with the head and neck exam for the detection of *oral disease*. This confusion is puzzling, as fluorescence visualization is intended to be, and is approved as, an adjunctive methodology for the detection of all oral mucosal abnormalities.

There have been some notable exceptions; Huff et al[9] conducted an interesting retrospective analysis comparing consecutive years in a private dental practice. During the second year a VELscope examination was added to the head and neck exam and ten dysplastic lesions were detected in the patient population as compared to none in the previous year. Most recently, a 620-patient study at the University of Washington[18] demonstrated that the addition of VELscope to routine clinical examinations resulted in the detection of a number of mucosal abnormalities not detected by the conventional exam. These abnormalities included a number of dysplasias, as well as lichen planus and other inflammatory lesions. The study highlights an aspect of fluorescence visualization that is often overshadowed by its role in the detection of oral dysplasia and cancer. Devices such as the VELscope provide general practitioners with a powerful tool to aid in the discovery of most types of oral lesions, such as viral, fungal and bacterial infections; inflammation from a variety of causes (including lichen planus and other lichenoid reactions); squamous papillomas, salivary gland tumours, etc.

CLINICAL EXAMPLES

The following clinical examples have been chosen to illustrate the above concepts.

Figure 1 illustrates an important point — automatically associating a loss of fluorescence with pathology is misguided. Note that the left tonsillar pillars, palatine tonsil and oropharynx are predominantly dark (i.e., show a "loss of fluorescence") because of absorption of light by the associated presence of vascularity and lymphoid tissue. Not

FIGURE 1—Normal factors such as vascularity and lymphoid tissue contribute to the spectrum of normal pattern variability under fluorescence visualization.

FIGURE 2—Trauma-associated inflammation on the left buccal mucosa. *(Images courtesy of the University of Washington Oral Medicine Program.)*

FIGURE 3—Loss of fluorescence under VELscope paired with observable inflammation under white light contributed to a diagnosis of oral candidiasis. *(Images courtesy of Dr. Samson Ng.)*

FIGURE 4—Fluorescence and white light confirm the resolution of candidiasis (as presented in Figure 3) after treatment. *(Images courtesy of Dr. Samson Ng.)*

Inflammatory changes from a wide variety of causes are relatively commonplace. Probably the most common occurrence is trauma-associated inflammation, as seen in this example on the left buccal mucosa (Fig. 2). The subtle visual appearance under white light is transformed, under VELscope, into two dramatic areas of loss of fluorescence that are difficult not to notice. Once seen, the fluorescence response together with the white light presentation paints a consistent picture of the underlying cause. The two dark patches correspond to the two mildly erythematous areas visible under white light. The vessel damage on the upper part of the buccal surface presents predictably as a dark area under fluorescence due to blood absorption, and is consistent with the picture of trauma from the teeth. Rather than being viewed as some sort of "false positive" or distraction, the fluorescence response should help focus the clinician on a legitimate (albeit non-life threatening) possibility of chronic trauma to the buccal mucosa, that may not have otherwise been noticed. This type of trauma can be caused by parafunctional habits, sharp or jagged cusps or malposed teeth, and could be addressed through counseling, oral appliances or smoothing of rough tooth surfaces.

This next case (Fig. 3) illustrates inflammation of a biological, as opposed to traumatic, origin. The patient had a history of asymptomatic red patches on the hard palate for the previous eighteen months. The loss of fluorescence and the erythematous, inflamed appearance under white light led the clinician to suspect candidiasis. Subsequent anti-fun-

all individuals, however, show this type of lymphoid aggregate proliferation. With a little experience, one becomes familiar with the spectrum of normal variation present in a wide cross-section of individuals seen in a typical dental practice. Lymphoid aggregates may become uniformly more prominent from inflammatory response; the clinician, however, should pay close attention to unilateral or asymmetrical changes as possibly suggestive of pathological change. The tak-

ing of fluorescence and conventional white light photographs, even of normal appearing tissue, facilitates this process by establishing a baseline against which future clinical and fluorescence presentations can be compared. Photographic documentation is an important part of the fluorescence visualization protocol, and is made possible by LED Dental's newest device, the VELscope Vx, designed to accommodate an optional, custom-built digital camera system.

gal therapy led to resolution in four weeks as shown below (Fig. 4).

The importance of always considering the results of the physical, visual and tactile examination in the context of the larger clinical picture is highlighted by consideration of the hard palates in these examples (Fig. 5).

Superficially, the cases in Figures 5a & 5b present similarly under both fluorescence and white light illumination, yet when evaluated together with patient history and risk factors, the picture that emerges is significantly different. The first patient complained of a sore mouth and reported sucking on hard candies. The second patient was asymptomatic, but had a number of risk factors (such as tobacco use and age) for the development of oral squamous cell carcinoma. In addition, subsequent follow-up resulted in complete resolution for patient 1, but no change for patient 2, confirming the clinician's intention to refer the second patient for biopsy, which detected the presence of dysplasia.

The three cases shown in Figures 6, 7 and 8 are all related to lichenoid tissue changes, but each has its own story to tell about the role of fluorescence in the oral mucosal diagnostic process. The first case (Fig. 6) presented with a subtle appearance under white light but demonstrated a striking loss of fluorescence when viewed through the VELscope. In addition to highlighting the presence of the lesion, fluorescence visualization also indicates a much larger area of mucosal involvement than suggested by the white light appearance. The juxtaposition of the le-

FIGURE 5A—These photos show an area of trauma caused by hard candy consumption. *(Images courtesy of the Benjamin Dental Group.)*

FIGURE 5B—These photos show a dysplastic lesion that demonstrates loss of fluorescence due to dysplasia. *(Images courtesy of the University of Washington Oral Medicine Program.)*

FIGURE 6—The juxtaposition of the lesion to the gold crown suggests a possible allergic lichenoid reaction. *(Images courtesy of Dr. Samson Ng.)*

FIGURE 7—Erosive lichen planus under fluorescence and white light. *(Images courtesy of the University of Washington Oral Medicine Program.)*

sion to the gold crown suggests a possible allergic lichenoid reaction to the metal, but the final decision regarding causation requires patch testing.

The case in Figure 7 presented clinically as would classic erosive lichen planus; patch testing on the patient failed to reveal any allergic reaction to typical den-

FIGURE 8—Fluorescence visualization helped answer the question — is this classic reticular lichen planus or a lichenoid reaction? *(Images courtesy of the University of Washington Oral Medicine Program.)*

FIGURE 9—This salivary gland tumour is difficult to visualize under white light but stands out under fluorescence visualization. *(Images courtesy of Dr. Samson Ng.)*

FIGURE 10—Fluorescence visualization helps bring this squamous papilloma to the attention of the clinician. *(Images courtesy of Dr. Samson Ng.)*

FIGURE 11—Classic example of an irregular area of loss of fluorescence associated with dysplasia. *(Images courtesy of Dr. Samson Ng.)*

metal restoration on the rear molar, but less so in other regions of the lichenoid reaction. This is clinically significant since the cause of the lichenoid response has a direct bearing on the therapeutic intervention: palliative use of topical steroids to treat the inflammation, as opposed to removing the cause of the allergic lichenoid reaction by replacing the metal restoration.

The distinct and localized loss of fluorescence observed on the hard palate of this patient (Fig. 9) is in striking contrast to the almost complete lack of colour or texture change as observed under white light. Although not evidenced by the white light photograph, there was a palpable bump corresponding to the area of loss of fluorescence. Biopsy confirmed the presence of a salivary gland tumour (low-grade mucoepidermoid carcinoma). This case demonstrates how loss of fluorescence can indicate serious abnormal pathology in the almost complete absence of other visual changes. (It also demonstrates the importance of palpating all oral structures when conducting the intra-oral soft tissue examination.) Note that fluorescence visualization played two roles: as an aid to discovery and to help confirm that this is a suspicious area warranting follow-up.

Another interesting facet of this case is that the lesion was not an epithelial-based cancer but originated from the salivary gland. It is postulated that the loss of fluorescence was caused by disruption of stromal collagen (breakdown of collagen cross-linking) brought about by tumour growth in the connective tissue layer. One might wonder if "benign" growths such as an

tal restorative materials. Notice how much better visualized the full inflammatory response of the tissue is under fluorescence, as compared to conventional illumination.

The case in Figure 8 initially presented under white light as a classic case of reticular lichen planus; fluorescence highlights the presence of an intense inflammatory response adjacent to the
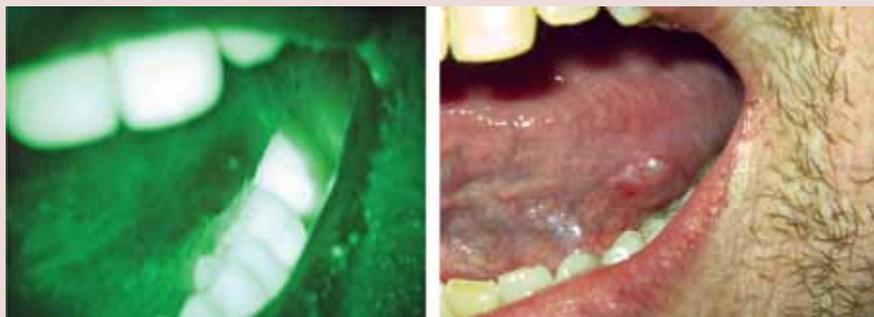
FIGURE 12—Even when lesions are clinically obvious under white light, fluorescence visualization helps in the confirmation process and provides additional information about the extent of the lesion. *(Images courtesy of the University of Washington Oral Medicine Program.)*

FIGURE 13—The loss of fluorescence exhibited in proximity to hyperkeratosis on the edentulous ridge was biopsy-confirmed as dysplasia. *(Images courtesy of the University of Washington Oral Medicine Program.)*

adenoma cause a loss of fluorescence. In fact, loss of fluorescence is likely to be a feature of both benign and malignant tumours, since both disrupt stromal collagen. An enlightened approach to the utility of fluorescence as a diagnostic tool would not regard this as a limitation, but as a useful feature; benign and malignant tumours require biopsy for definitive diagnosis and both require therapeutic intervention.

Figure 10 illustrates another example of how an unremarkable appearance under white light can correspond to an obvious abnormality with fluorescence. This particular lesion is a squamous papilloma which must be biopsied for definitive diagnosis and then is typically excised. Note that earlier discovery and diagnosis leads to less invasive intervention for the patient.

This somewhat clinically obvious lesion in the floor of mouth (Fig. 11) is a classic example of a large, irregular area of loss of fluorescence corresponding to precancerous dysplasia. Note the highly asymmetric nature of the lesion when viewed through the VELscope, as well as the irregular, well-defined border — an abnormal fluorescence pattern highly suggestive of precancerous or cancerous changes.

This example of a dysplastic lesion on the lateral border of the tongue (Fig. 12) highlights the added clinical value that the VELscope can bring even when the main part of the lesion is clinically obvious. In this case the area of loss of fluorescence extended at least 10-15mm anterior to the main, clinically apparent part of the lesion, and was also biopsy-confirmed as dysplasia.

This final example (Fig. 13) illustrates how the VELscope can bring the clinician's attention to an area that might otherwise be overlooked. At first sight, this appeared to be a case of denture trauma with inflammation in the vestibule, as well as hyperkeratotic areas apparent on the edentulous ridge. However, the striking loss of fluorescence corresponding to the hyperkeratosis on the ridge (in the absence of any other clinical signs of inflammation) is highly suspicious, and alerted the clinician to biopsy the area. This resulted in a diagnosis of dysplasia.

When fluorescence visualization devices such as the VELscope are used in their proper clinical context, adjunctively and as part of the complete diagnostic protocol, including patient history and the traditional head and neck exam using white light and palpation, general dentistry practices are provided with a new perspective on the health of oral mucosal tissues. Beyond the dramatic and profound benefits of early dysplasia and cancer detection, examination including fluorescence visualization can assist dentists and hygienists in bringing their patients closer to a state of "total oral health," with its corollary systemic benefits.

David Morgan is Chief Science Officer at LED Dental Inc. and has 15 years of R&D and product development experience in the use of fluorescence as an aid to disease detection.

clinical images and reviewing the manuscript.

Oral Health welcomes this original article.

REFERENCES

1. Lane PM, Gilhuly T, Whitehead P, Zeng H, Poh CF, Ng S, Williams PM, Zhang L, Rosin MP, MacAulay CE. Simple device for the direct visualization of oral-cavity tissue fluorescence. J Biomed Opt 2006;11(2):024006.
2. Kois J, Truelove E. Detecting oral cancer: a new technique and case reports. Dent Today 2006;25:96-7.
3. Poh CF, Zhang L, Anderson DW, Durham JS, Williams PM, Priddy RW, Berean KW, Ng S, Tseng OL, MacAulay C, Rosin MP. Fluorescence visualization detection of field alterations in tumor margins of oral cancer patients. Clin Cancer Res 2006;12(22):6716-6722.
4. Poh CF, Ng SP, Williams PM, Zhang L, Laronde DM, Lane P, Macaulay C, Rosin MP. Direct fluorescence visualization of clinically occult high-risk oral premalignant disease using a simple hand-held device. Head Neck 2007;29(1):71-76.
5. "Direct Fluorescence Visualization as Adjunct for Identification of High-Risk Oral Premalignancies", Zhang et al, AACR Poster Presentation, April 2007.
6. Poh CF, Ng S, Berean KW, Williams PM, Rosin MP, Zhang L. Biopsy and Histopathologic Diagnosis of Oral Premalignant and Malignant Lesions. J Can Dent Assoc. 2008 Apr;74(3):283-8.
7. Williams PM, Poh CF, Hovan AJ, Ng S, Rosin MP. Evaluation of a suspicious oral mucosal lesion. J Can Dent Assoc. 2008 Apr;74(3):275-80.
8. "A Real-Time Application of Fluorescence Visualization (FV) to Identify a Novel Optical Field for Subclinical Extension in High-Risk Oral Lesions", Poh et al, AAOMP Oral Presentation, June 2008.
9. Huff K, Stark PC, Solomon LW. Sensitivity of direct tissue fluorescence visualization in screening for oral premalignant lesions in general practice. Gen Dent 2009;57(1):34-38.
10. Poh CF, MacAulay CE, Zhang L, Rosin MP. Tracing the "At-Risk" Oral Mucosa Field with Autofluorescence: Steps Toward Clinical Impact. Cancer Prev Res 2009;2(5):402:404.
11. Pautke C, Bauer F, Tischer T, Kreutzer K, Weitz J, Kesting M, Hölzle F, Kolk A, Stürzenbaum SR, Wolff KD. Fluorescence-guided bone resection in bisphosphonate-associated osteonecrosis of the jaws. J Oral Maxillofac Surg. 2009 Mar;67(3):471-6.
12. Pautke C, Bauer F, Bissinger O, Tischer T, Kreutzer K, Steiner T, Weitz J, Otto S, Wolff KD, Stürzenbaum SR, Kolk A. Tetracycline bone fluorescence: a valuable marker for osteonecrosis characterization and therapy. J Oral Maxillofac Surg. 2010 Jan;68(1):125-9.
13. Pautke C, Bauer F, Otto S, Tischer T, Steiner T, Weitz J, Kreutzer K, Hohlweg-Majert B, Wolff KD, Hafner S, Mast G, Ehrenfeld M, Stürzenbaum SR, Kolk A. Fluorescence-guided bone resection in bisphosphonate-related osteonecrosis of the jaws: first clinical results of a prospective pilot study. J Oral Maxillofac Surg. 2011 Jan;69(1):84-91. Epub 2010 Oct 25.
14. Mehrotra R, Singh M, Thomas S, Nair P, Pandya S, Nigam NS, Shukla P. A cross-sectional study evaluating chemiluminescence and autofluorescence in the detection of clinically innocuous precancerous and cancerous oral lesions. J Am Dent Assoc 2010;141(2):151-156.
15. Scheer M, Neugebauer J, Derman A, Fuss J, Drebber U, Zoeller J. Autofluorescence imaging of potentially malignant mucosa lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:568-577.
16. Awan K, Morgan PR, Warnakulasuriya S. Evaluation of an autofluorescence based imaging system (VELscope™) in the detection of oral potentially malignant disorders and benign keratosis. Oral Oncol 2011; 47(4):274-7.
17. Farah CS, McIntosh L, Georgiou A, McCullough MJ. Efficacy of tissue autofluorescence imaging (velscope) in the visualization of oral mucosal lesions. Head Neck. 2011 Aug 4. doi: 10.1002/hed.21834.
18. Truelove EL, Dean D, Maltby S, Griffith M, Huggins K, Griffith M, Taylor S. Narrow band (light) imaging of oral mucosa in routine dental patients. Part I: Assessment of value in detection of mucosal changes. Gen Dent 2011; 59(4): 282-289.
19. Lingen LW, Kalmar JR, Karrison T, Speight PM. Critical evaluation of diagnostic aids for the detection of oral cancer. Oral Oncol. 2008 Jan;44(1):10-22. Epub 2007 Sep 6.
20. Patton LL, Epstein JB, Kerr AR. Adjunctive techniques for oral cancer examination and lesion diagnosis: A systematic review of the literature. J Am Dent Assoc 2008;139(7):896-905.
21. Rethman MP, Carpenter W, Cohen EE, Epstein J, Evans CA, Flaitz CM, Graham FJ, Hujoel PP, Kalmar JR, Koch WM, Lambert PM, Lingen MW, Oettmeier BW Jr, Patton LL, Perkins D, Reid BC, Sciubba JJ, Tomar SL, Wyatt AD Jr, Aravamudhan K, Frantsve-Hawley J, Cleveland JL, Meyer DM; American Dental Association Council on Scientific Affairs Expert Panel on Screening for Oral Squamous Cell Carcinomas. Evidence-based clinical recommendations regarding screening for oral squamous cell carcinomas. J Am Dent Assoc 2010 May;141(5):509-20.