

Detection of Oral Pathologies Using Optical Coherence Tomography

a report by

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DOI: 10.17925/EOH.2008.04.1.57

Optical biopsy techniques can provide immediate *in vivo* diagnosis of suspicious oral lesions. Other advantages include their non-invasive nature and reducing patient stress and anxiety while waiting for the diagnosis. Some of these techniques have already been incorporated into clinical practice and have become indispensable tools in oral dysplasia clinics (e.g. fluorescence spectroscopy); others continue to be applied in clinical research studies and results show great promise for their use in clinical practice in the near future (e.g. elastic scattering spectroscopy, microendoscopy and optical coherence tomography).¹⁻⁸

Pre-malignancy and Oral Cancer

Early detection and management of pre-malignant oral lesions can significantly reduce the progression of these lesions into invasive cancer, and would thus reduce morbidity and mortality. This is usually augmented by patient counselling and advice on the reversal of habits that increase the risk of developing cancer (e.g. smoking and drinking).⁹⁻¹¹

A pre-malignant lesion is always at risk of malignant transformation if certain exogenous factors or conditions persist. Regular monitoring of these lesions is mandatory; when suspicious of neoplastic transformation, a biopsy may be required. This can be uncomfortable, time-consuming, costly and stressful to the patient while waiting for the diagnosis.^{1,2,4,8}

Oral cancer is the sixth most common cancer worldwide; it represents about 2% of cancers in the UK, with an incidence of 5.9/100,000 and a prevalence of one in 1,000. There are about 3,500 new cases per year, with a death rate of over 50%. The overall death rate in all cases is 54% (the highest is in tongue cancer at 60%, followed by intra-oral cancer at 56%, and the lowest is in lip cancer at 14%).⁹⁻¹³

Oral cavity cancers are more common in males, with a male-to-female ratio of 3-4:1. Tobacco and alcohol have multiplicative effects on oral cancer. The addition of poor oral hygiene and poor dentition can increase the risk eight-fold.⁹⁻¹³

The most common presentation of cancer of the floor of the mouth is a painless inflamed superficial ulcer with poorly defined margins. Pre-existent or coincident leukoplakia can be observed in adjacent tissues. The presence of erythroplakia strongly suggests a possible invasive tumour with malignant transformation. A small ulceration or nodular lesion may remain asymptomatic for long periods, so the patient may not seek medical attention.^{1,9-11}

Visual Examination and Histopathology

There is a strong clinical need to improve the early detection of pre-malignant oral lesions in order to enable earlier successful intervention

with less aggressive therapy, resulting in improved rates of morbidity and mortality.⁹⁻¹¹

Conventional visual examination and palpation remains the subjective 'gold standard' for the identification of abnormal oral mucosal lesions. Clinical differentiation of lesions is usually based on morphological changes in tissues; clinical experience is usually considered to be a major factor in its success. However, it has been found to be less sensitive in differentiating between lesions with similar clinical and morphological characteristics, e.g. dysplasia and carcinoma *in situ*.¹

Histopathology continues to be the complementary objective 'gold standard' to visual examination in the diagnosis of abnormal oral lesions. Parameters like disorganised epithelial orientation and architecture; changes in the morphology of the epithelial surface and thickness; alteration in nuclear size and morphology; and alteration in the nuclear/cytoplasmic ratio, cellular crowding and chromatin pattern can guide the pathologist to easily identify a pre-malignant lesion. A breach of the basement membrane indicates an invasive cancer.^{1,2,7} Other diagnostic techniques usually used to aid diagnosis, staging and monitoring include ultrasound, magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET).

Optical Biopsy – An Emerging Modality

Over past decades, researchers have investigated the possibility of developing a realtime, *in situ*, non-invasive technique that can aid in the diagnosis of abnormal tissue (i.e. inflammation, hyperkeratosis, ischaemia, metaplasia, dysplasia and neoplasia). The use of light (optical biopsy) in the diagnosis of tissue pathology represented a leap into the future. The aim was to develop a technique that could act as an adjunct or even replace histopathology and thus reduce surgical

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Figure 1: Swept-source Fourier-domain Optical Coherence Tomography Provided by Michelson Diagnostics (left), Sample Arm Scanning Laser and a Digital Camera (top right) and Manually Adjustable Stage to Facilitate Scanning of the Tissue Sample (bottom right)

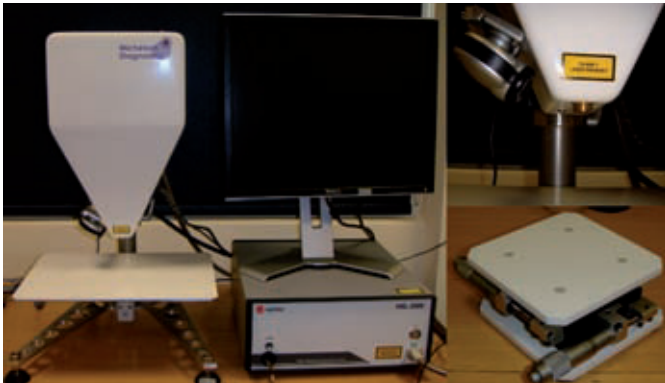
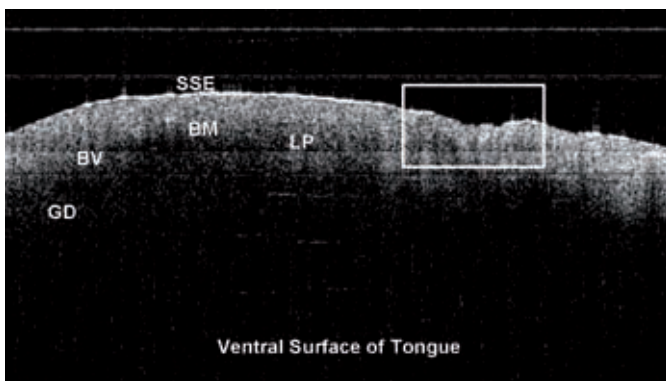


Figure 2: Speckled Erythroplakia of the Dorsal Tongue, Strongly Suggestive of Oral Cancer



Figure 3: Optical Coherence Tomography Image of the Ventral Surface of the Tongue

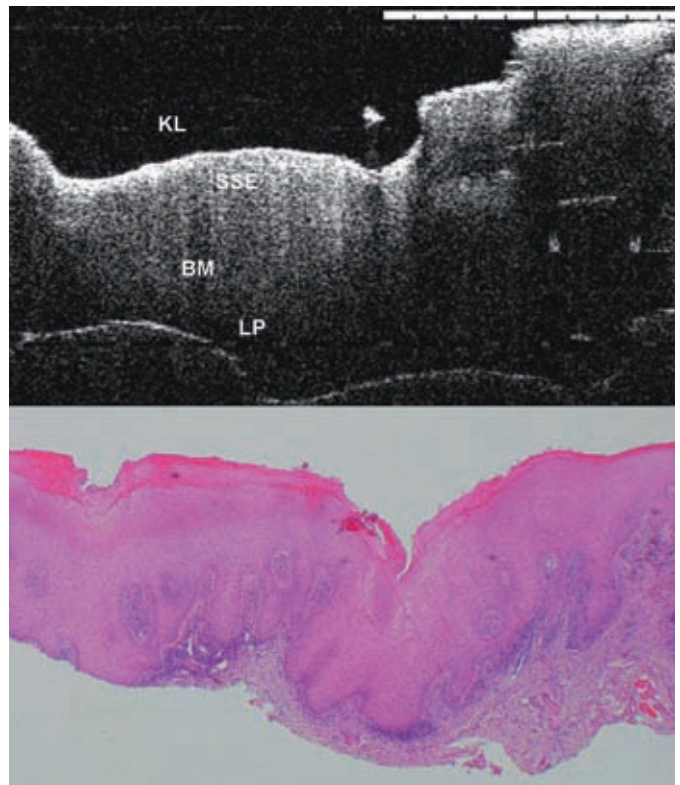


The area in the box shows a focal disruption of the surface keratin layer and mild thinning (atrophy) of the epithelium. BM = basement membrane; BV = blood vessel; GD = glandular duct; LP = lamina propria; SSE = stratified squamous epithelium.

trauma and the workload of already strained pathology departments and services.¹⁻³

Optical biopsies can be acquired through different modalities; each has its own mechanism of action and requires different modes of data analysis. Several optical diagnostic techniques have been employed with variable success rates. The main techniques currently utilised in the detection of oral dysplasia are fluorescence, Raman spectroscopy,

Figure 4: Hyperkeratosis with Lichenoid Reaction of the Lateral Border of the Tongue Illustrated by Optical Coherence Tomography (top) and Conventional Histology (bottom)



H+E x 20 magnification. Optical coherence tomography (OCT) shows thickening of the keratin layer, associated with epithelial hyperplasia and focal thickening of the basement membrane. These features corresponded to conventional histology images. BM = basement membrane; KL = keratin layer; LP = lamina propria; SSE = stratified squamous epithelium.

microendoscopy, elastic scattering spectroscopy and optical coherence tomography.^{1-8,14-16} Elastic scattering spectroscopy (ESS) has proved to be a promising method for detecting pre-malignant and malignant changes in oral tissues with high sensitivity and specificity. Several head and neck tissues, including lymph nodes and bones, have been interrogated using ESS, which detects changes at the cellular and subcellular level, with very promising results.^{2,5-7} Fluorescence spectroscopy, unlike ESS, can identify changes through the fluorophores detected in the tissue, and has been found to be very accurate in detecting oral dysplasia.⁴ Raman spectroscopy can detect biochemical changes in tissue, but it has limited clinical applications due to its weak signal. The first application of microendoscopy in the head and neck was described by Upile et al. at University College Hospital, London: resected tumour margins were examined and the results were impressive; however, a fundamental understanding of histopathology is essential for achieving a high sensitivity and specificity.⁸

Optical Coherence Tomography

Optical coherence tomography (OCT), first applied in 1991 by Huang et al., is a non-invasive, interferometric (superimposing or interfering waves) tomographic imaging modality that allows millimetre penetration with micrometre-scale axial and lateral resolution. The time-resolved technique is extensively used clinically in ophthalmology. OCT has been applied in the head and neck in an attempt to detect areas of inflammation, dysplasia and cancer; results were promising,

but some studies suffered from poor-resolution images and poor penetration depth.^{14–16}

Successful Optical Coherence Tomography Studies on Head and Neck Tissues

Ridgway et al. examined the mucosa of the oral cavity and the oropharynx using OCT in 41 patients during operative endoscopy. OCT imaging was combined with endoscopic photography for gross and histological image correlation. They found that OCT images of

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the oral cavity and oropharynx provided microanatomical information on the epithelium, basement membrane, and supporting lamina propria of the mucosa. OCT imaging showed distinct zones of normal, altered and ablated tissue microstructures for each pathological process studied.¹⁴

Armstrong et al.¹⁵ evaluated the ability of OCT to identify the characteristics of laryngeal cancer and measurable changes in the basement membrane, tissue microstructure, and the transition zone at the edge of tumours in 26 OCT examinations. OCT clearly identified basement membrane violation from laryngeal cancer and could identify transition zones at the cancer margin. They suggested that OCT showed potential for assisting in diagnostic assessment.

Wong et al.¹⁶ performed OCT imaging on 82 patients who underwent surgical endoscopy for various head and neck pathologies. They concluded that OCT has the unique ability to image laryngeal tissue microstructure and can detail microanatomical changes in benign, pre-malignant and malignant laryngeal pathologies.

A recent study carried out at the National Medical Laser Centre, University College London and the Head and Neck Unit, University College Hospital used the swept-source frequency-domain optical coherence tomography microscope (Michelson Diagnostics EX1301

OCT Microscope V1.0) (see *Figure 1*) to compare findings of OCT with histopathology of various oral lesions to see whether this technique could be used as an adjunct to histopathology in assessing oral leukoplakias and erythroplakias (see *Figure 2*).

Twenty-four oral lesions from 19 patients with suspicious oral lesions were excised and subjected to OCT. The acquired OCT images were then compared with histopathology images. Epithelium, basement membrane, lamina propria, microanatomical histological structures and pathological processes were clearly identified. Normal microanatomical structures identified in these tissues included the overlying keratin layer, papillae, ducts, glands and blood vessels. Regions of pathological features studied included leukoplakias and erythroplakias (see *Figure 3*). Areas of architectural changes were clearly visible and correlated well with the histopathological slides to a depth of approximately 1.5mm (see *Figure 4*). It was concluded that OCT can identify various histological structures as well as pathological changes that occur in these tissues.

The Future

OCT is a new optical modality that may be used alone or in combination with other optical-based systems to aid diagnosis and monitor treatment. OCT imaging of suspicious oral lesions could improve the diagnostic accuracy for oral dysplasia and the differential

Optical coherence tomography imaging of suspicious oral lesions could improve the diagnostic accuracy for oral dysplasia and the differential diagnosis between neoplastic and non-neoplastic lesions.

diagnosis between neoplastic and non-neoplastic lesions. Sampling for histological analysis could be better targeted.

If this technology were to be applied as screening or as part of diagnostic programmes in clinical practice in the coming years, this might reduce morbidity and mortality in large populations of patients, especially those with treated oropharyngeal/laryngeal cancer. ■

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