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Optical coherence tomography in the assessment of oral squamous cell carcinoma resection margins

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ABSTRACT

Background: Incomplete surgical removal of cancer is believed to be the main cause of local recurrence and high mortality. This study assessed the use of optical technology (namely optical coherence tomography [OCT]) in examining oral squamous cell carcinoma (OSCC) resection margins to assess if this modality could guide the surgeon during surgical resections.

Materials and methods: Twenty-eight T_1–T_2 N0M0 oral squamous cell carcinoma patients participated in this study. Nineteen patients were males and nine were females. The majority of lesions were in the ventro-lateral tongue, floor of mouth, retromolar trigone and the buccal mucosa.

Following tumour resection, the specimen resection margins were optically scanned in the immediate ex vivo phase. Two independent assessors commented on the four resection margins of each specimen. The findings were then compared to the corresponding gold standard histopathology. The average epithelial thickness for both tumor-free and tumor-involved margins was also calculated.

Results: The pathology reports of the 112 margins revealed 90 tumor-free margins and 22 tumor-involved margins. Examining the data from both senior operating surgeons (assessors), the overall sensitivity and specificity was found to be 81.5% and 87%, respectively. Whilst the positive predictive value was 61.5% and the negative predictive value was 95%. OCT accuracy for the first assessor was 88% and for the second assessor 84%. The assessors' inter-observer agreement was "very good" for superior, inferior and medial margins; while agreement on the lateral surgical margin status was "good". Using OCT, the mean epithelial thickness at the tumor-free resection margins was 360 μm; while, it was 567 μm for the tumour-involved margins.

Conclusion: OCT is a valuable tool in the assessment of surgical margins. Tumour-involved margins can be identified by architectural changes and increase in epithelial layer thickness on the OCT image. Further studies are required to assess tumour margins in vivo.

1. Introduction

The UK guidelines judge both mucosal and deep margins of ≥5 mm free of tumour as clear, 1–5 mm as close and ≤1 mm as involved. This usually ignores the formalin-shrinkage effect, which can reach up to 30%. So in order to achieve a 5 mm pathological clearance, 8–10 mm in situ surgical margin, a considerable amount of normal tissue needs to be taken [1].

Positive (tumour-involved) or close margins are associated with increase in local recurrence with an attendant negative effect on survival. Although there is lack of high evidence-based publications that show a significant correlation between close resection margins and negative outcomes when it comes to survival and recurrence, several studies have shown that local recurrence and overall survival benefit from achieving negative resection margins [1–4].

One of the unresolved clinical issues is the absent of any objectively reliable and accurate assessment modality for resection margin status. In most cases, intraoperative visual inspection and palpation is the standard approach. Unfortunately, this technique resulted in positive or close surgical margins in almost 40% of the patients, in one study [2]. Intraoperative frozen sections, although widely used, has its own inherited problems. This technique is

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costly, time consuming. Additionally, the frozen samples do not represent the whole margins but random sampling; which may misrepresent the real situation [3,4]. To help overcome these clinical challenges, a highly sensitive, non-invasive, cost-effective and in vivo diagnostic tool is required.

The use of optical technology (diagnostics) in clinical trials has increased in the past few years. If found to be effective; these tools can help by reducing pathology workload and by acting as adjunct to pathology in specific situations. Optical coherence tomography (OCT) is one of these diagnostic tools that hold great promise. Huang et al. have pioneered the principle of OCT in 1990s [5]. Its clinical use was, initially, restricted to the field of ophthalmology [6]. Soon after, its clinical application expanded to involve several body tissue pathologies [7–9]. In head and neck, OCT has been used to detect early epithelial changes in the oropharyngeal/laryngeal region. Prestin et al. [10] in a study measuring oral tissue epithelium using OCT found that it was feasible to identify oral malignancy and determine the approximate grade of dysplasia.

In a preliminary immediate ex vivo study carried out by our group on oral tissues, we compared findings of optical coherence tomography (OCT) with histopathological results of suspicious oral lesions. Thirty-four oral lesions from 27 patients were subjected to swept-source frequency-domain OCT. OCT could identify diseased areas but could not provide a diagnosis or differentiate between abnormal lesions of close pathological characteristics (i.e. different grades of dysplasia and carcinoma in situ). Overall, the pilot study, by Jerjes et al., confirmed the feasibility of using OCT to identify architectural changes in malignant tissues [11].

Previous studies using different OCT systems confirmed the effectiveness of such diagnostic technology but the generated images were of low resolution due to poor penetration depth and lateral resolution. Wilder-Smith et al. [12] evaluated the clinical capability of non-invasive in vivo OCT for diagnosing oral dysplasia and malignancy in 50 patients. Their data demonstrated good capability of the in vivo OCT but have suffered from resolution problems. An earlier study by Ridgway et al. [13] outlined future applications of OCT technology by examining the mucosa of the oral cavity and oropharynx in 41 patients during operative endoscopy. Optical coherence tomographic imaging showed distinct zones of normal, altered, and ablated tissue microstructures for each pathologic process studied.

In laryngology, OCT was found to be efficient, quick, and reliable imaging modality in guiding surgical biopsies, intraoperative decision making, and therapeutic options of various laryngeal pathologies [14]. A prospective study by Just et al. [15] assessed OCT application in benign and dysplastic laryngeal epithelial lesions. They showed that the thickness of the epithelium is the main criterion for degree of dysplasia. In their study, OCT provided test outcomes for differentiation between benign laryngeal lesions and dysplasia/CIS with sensitivity of 88% and specificity of 89%. However, and due to the limited penetration depth of the laser light in hyperkeratotic lesions, the basal cell layer was no longer visible, preventing reliable assessment of such lesions.

An interesting study by Kraft et al. [16] using microlaryngoscopy with OCT during the diagnostic investigation and intraoperative monitoring of laryngeal disease presented a higher sensitivity in predicting invasive tumor growth and epithelial dysplasia, when compared to microlaryngoscopy alone. A recent pilot study by Conti de Freitas et al. [17] looked at resection margins and demonstrated that OCT is capable of recognizing and differentiating neck tissues encountered during thyroid and parathyroid surgeries.

The aim of this immediate ex vivo clinical study was to assess the role of OCT in identifying tumour-involved resection margins in patients undergoing surgery for oral squamous cell carcinoma (OSCC). Epithelial layer thickness and architectural changes were the main parameters assessed at each of the resection margins.

Table 1
Demographics of the cohort included in this study.

	No. (%)		No. (%)
Gender		Symptoms	
Male	19 (67.9)	Asymptomatic	19 (67.9)
Female	9 (32.1)	Pain	4 (14.3)
		Bleeding	5 (17.9)
Location			
Ventro-lateral tongue	7 (25.0)	Smoking status	
Floor of mouth	6 (21.4)	Current smoking	10 (35.7)
Retromolar trigone	4 (14.2)	Ex-smoker	12 (42.9)
Buccal mucosa	3 (10.7)	Non-smoker	6 (21.4)
Lower lip	2 (7.1)		
Hard palate	2 (7.1)	Drinking status	
Upper lip	2 (7.1)	Current drinker	12 (42.9)
Soft palate	2 (7.1)	Ex-drinker	6 (21.4)
		Non-drinker	10 (35.7)
Colour			
Leukoplakia	4 (14.3)	Pan chewing	3 (10.7)
Erythroplakia	14 (50.0)		
Speckled leukoplakia	10 (35.7)	Diagnosis	
		T_1 disease	20 (71.4)
Clinical features		T_2 disease	8 (28.6)
Plague	6 (21.4)		
Papule	6 (21.4)	Resection	
Ulcer	16 (57.1)	CO_2 Laser	7 (25.0)
		Surgical resection	17 (60.7)
Medical history		Electrosurgical	4 (14.3)
ASA I	20 (71.4)		
ASA II	8 (28.6)		

2. Materials and methods

Identical protocols were used to recruit 28 consecutive patients who presented with suspicious oral lesions to the UCLH Head and Neck Centre, London between 2008 and 2010. The study protocol was approved by the Committee of the Ethics for Human Research.

Nineteen patients were males (67.9%) and nine were females (32.1%); with a mean age of 61 years (range 36–103 years). Approximately one-third of the patients were current smokers. Over 40% of the patients consumed alcohol on a regular basis and less than 10% chewed betel nut (Table 1). Half of the lesions were ulcers; and the rest manifested as plaques or papules. Fifty percent ($n = 14$) of the lesions manifested as erythroplakia, 35.7% presented as leukoerythroplakia and 14.3% as homogeneous leukoplakia. The anatomical distribution of the lesions showed 7 in the ventro-lateral tongue, 6 in the floor of mouth, 4 in retromolar trigone and 3 in the buccal mucosa (Table 1).

An incisional surgical biopsy was acquired from each patient and confirmed the diagnoses of oral squamous cell carcinoma (OSCC). Clinical staging at time of presentation showed that 20 patients had T1N0 disease [mean depth of invasion 4.6 mm, minimum 1.2 mm, maximum 6.3] and 8 patients had T2N0 disease [mean depth of invasion 5.8 mm, minimum 1.4 mm, maximum 9.6]. All patients were discussed at our multi-disciplinary meeting, and the ones with deep malignancies invading >5 mm, although with clinical N0 necks, were recommended for further intervention in the form of selective neck dissection to ensure loco-regional control. The presence of moderate or severe dysplasia at margin is strongly correlated with inferior local control and potentially worse disease-free survival and hence [18], any patient in our study that fits this description received postoperative radiotherapy and/or chemotherapy as a result.

A “pre-made proforma” was used to collect clinic-pathological and optical data from each patient included in this study. We