

# Management of oral carcinoma: benefits of early precancerous intervention

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Accepted 5 December 2009

Available online 1 August 2010

## Abstract

Management of oral precancerous lesions remains polarised between interventional surgery and conservative treatment. We have previously shown the efficacy of carbon dioxide laser excision for both diagnosis and treatment of oral precancerous lesions. The aim of this study was to review the clinicopathological details of a group of patients in whom pre-existing but occult invasive carcinoma was diagnosed histopathologically in specimens excised by laser. We retrospectively reviewed 169 patients who attended the Maxillofacial Dysplasia Clinic at Newcastle General Hospital with single, new oral premalignant lesions over a 5-year period (2004–2008). They were all treated by laser excision of lesions that were confirmed to be dysplastic from examination of preoperative incisional biopsy specimens. There was a significant correlation between the results of diagnostic incisional, and laser excision, biopsy specimens ( $p < 0.01$ ), but 15 patients had signs of occult invasive carcinoma in the excision specimens (9%). In all cases the carcinomas were completely excised by the laser. Carbon dioxide laser excision is not only an effective treatment of precancerous lesions, but also facilitates early diagnosis and management of oral carcinoma at a stage when it is otherwise clinically undetectable.

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*Keywords:* Precancer; Carcinoma; Laser

## Introduction

The management of oral precancerous lesions remains controversial, and a lack of prospective, randomised, controlled trials means that there are no formally approved evidence-based treatments. We have previously described the efficacy of excision with a carbon dioxide laser in both the diagnosis and treatment of premalignant oral lesions.<sup>1,2</sup>

The decision whether or not to excise dysplastic lesions is influenced by the perceived risk of malignant transformation, but quoted figures for the development of oral squamous cell carcinoma (SCC) vary between 0.13 and 36.4%.<sup>3</sup> One of the most useful prognostic indicators remains the severity of epithelial dysplasia, with the most severely dysplastic

lesions at greatest risk of transformation.<sup>4–9</sup> Many clinicians consider that lesions that show moderate or severe dysplasia should be excised, but we also recommend excision of mildly dysplastic lesions at high risk sites in young patients, particularly those who continue to smoke or who are unlikely to attend for regular follow up.

The severity of dysplasia was primarily assessed by histological examination of an incisional biopsy specimen, and categorised according to features defined by the WHO, classically into mild, moderate, and severe.<sup>10</sup> Discrepancies have been reported, however, between diagnoses obtained from incisional biopsy specimens and resection specimens.<sup>1,3</sup> These may be the result of inadequate sampling of lesions when initially biopsied, or to subjective differences in histopathological interpretation.<sup>11–13</sup> Of particular importance is the identification of more obvious dysplasia or frankly invasive oral SCC in excision specimens.

Oral SCC is not commonly identified until lesions are of sufficient size to be clinically evident or symptomatic. It

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Table 1  
Relation between results of incisional and excisional biopsies ( $n = 169$ ).

Dysplasia present in incisional biopsy	Excisional biopsy showing dysplasia or oral SCC			
	Mild	Moderate	Severe	Oral SCC
Mild	46	22	5	1
Moderate	8	25	21	6
Severe	0	4	23	8

remains unclear whether oral SCCs develop from dysplastic oral mucosa or de novo without identifiable pre-existing precancerous changes. Occult oral SCC detected in excisional biopsy specimens of dysplastic tissue may support the ‘dysplasia progression’ model, but the clinicopathological features of patients with occult oral SCC have not been well-documented, largely because of difficulties in monitoring large groups of patients with dysplasia. Incisional biopsy may not provide a representative sample of tissue from which the degree of dysplasia or presence of oral SCC can be assessed, so rates of malignant transformation might be more accurately measured from excision biopsy specimens.

To address some of the deficiencies related to ‘underdiagnosis’ from incisional biopsy specimens, the aims of this study were: to evaluate the clinicopathological features of a group of patients with dysplastic lesions in whom excision biopsy specimens showed ‘unexpected’ oral SCC; and to review the correlation between diagnoses of dysplasia from incisional and excisional biopsy specimens.

## Patients and methods

We retrospectively reviewed 169 consecutive new patients with single oral precancerous dysplastic lesions who presented between January 2004 and December 2008 to the Maxillofacial Dysplasia Clinic at Newcastle General Hospital.

Patients with multiple lesions were excluded, as were those who presented with oral SCC and patients who waited more than 6 weeks between incision biopsy and laser excision.

All patients had an interventional management protocol that comprised identification of risk factors (such as consumption of alcohol and smoking habits by way of structured medical and social histories) followed by incisional biopsy and laser excision by a single surgeon working to an established protocol.<sup>1,2</sup> Incisional and excisional biopsy specimens were evaluated for the degree of dysplasia or presence of oral SCC by the same team of experienced oral pathologists.

The following features were recorded for patients with oral SCC: clinical details, appearance and anatomical site of lesions, degree of dysplasia on incisional biopsy, dimensions of any dysplasia seen in excision specimens, and histopathological features of excised oral SCCs.

Overall correlation between the results of incisional and excisional biopsy specimens was made using Pearson’s correlation coefficient aided by the Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL).

## Results

A total of 169 patients (76 female and 93 male; mean age 57 years, range 33–77) had incisional biopsy and subsequent laser excision of dysplastic lesions during the period specified.

Table 1 shows the relations between initial, diagnostic incisional biopsy specimens and their laser excision counterparts for 169 lesions. Overall, in 94 patients (56%) there was agreement between incision and excision histological diagnoses ( $r = 0.678$ ;  $p < 0.01$ ).

Fifteen patients (9%), however, were found to have ‘unexpected’ invasive carcinoma in the excised specimens, with a further 48 (28%) showing more obvious dysplasia in full excisions compared with diagnoses from incisional biopsy specimens.

In 11 patients (7%) the most important regions of dysplasia were apparently identified and removed during incisional biopsy before laser excision, as histological examination of the excision specimen showed less severe dysplasia.

Table 2 lists the clinicopathological features of the 15 patients who were found to have unexpected oral SCC in their laser excision specimens; there were 9 men (mean age 57.4 years, range 49–66) and 6 women (mean age 59.5 years, range 33–77), with no significant age or sex differences.

Laser excision specimens had mean dimensions of 26.7 mm long  $\times$  15.2 mm wide  $\times$  5.8 mm deep. Foci of oral SCC were small, with mean dimensions of 2.9 mm in diameter by 1.8 mm deep, and were primarily well-differentiated carcinomas showing superficial or early invasive features. The 5 moderately differentiated carcinomas all arose from lesions that had shown severe dysplasia on incisional biopsy. All oral SCCs were completely excised by laser with a margin of 5 mm or more; no local recurrences or regional metastases were seen during a mean (SD) follow up 36.2 (6.5) months.

## Discussion

Oral SCC is a lethal and deforming disease, which is still characterised by late presentation of advanced intraoral tumours

Table 2  
Clinical and histopathological features of unexpected SCC.

Case no.	Age	M/F	O/E	Site	IB histology	EB size (mm)	Margins	Type of SCC (size, mm)	Invasive front
1	33	F	L	Tongue dorsum	Verruciform hyperplasia; mild dysplasia	30 × 19 × 6	Clear (CE)	WD (5 × 2)	Early invasive
2	49	M	L	Lateral tongue	Severe dysplasia	24 × 15 × 6	Clear (CE)	WD (2 × 2)	Early invasive
3	49	F	L	Lateral tongue	Moderate dysplasia	45 × 22 × 7	Clear (CE)	WD (2 × 2)	Early invasive
4	51	M	L	Floor of mouth	Severe dysplasia	31 × 20 × 6	Clear (CE)	MOD (1.5 × 2)	Early invasive
5	52	M	L	Ventral tongue	Moderate dysplasia	32 × 15 × 8	Clear (CE)	WD (3 × 1)	Early invasive
6	56	M	L	Floor of mouth	Severe dysplasia	45 × 25 × 12	Close	MOD (10 × 4)	Early invasive
7	59	F	EL	Soft palate	Severe dysplasia	17 × 11 × 4	Close	WD (2 × 1)	Early invasive
8	59	M	EL	Labial mucosa	Moderate dysplasia	15 × 13 × 4	Clear (CE)	WD (1 × 1)	Early invasive
9	61	M	L	Tongue dorsum	Severe dysplasia	24 × 12 × 3	Clear (CE)	MOD (3 × 2)	Early invasive
10	61	M	EL	Floor of mouth	Moderate dysplasia	11 × 6 × 3	Severe dysplasia	WD (2 × 1)	Superficially invasive
11	62	M	E	Soft palate	Severe dysplasia	22 × 17 × 5	Clear (CE)	WD (2 × 0.8)	Early invasive
12	65	F	EL	Floor of mouth	Severe dysplasia	25 × 10 × 2	Clear (CE)	MOD (1 × 1.5)	Superficially invasive
13	66	M	EL	Ventral tongue	Moderate dysplasia	45 × 19 × 7	Clear (CE)	WD (6 × 2)	Early invasive
14	74	F	L	Lateral tongue	Moderate dysplasia	26 × 17 × 6	Clear (CE)	WD (2 × 2)	Early invasive
15	77	F	L	Lateral tongue	Severe dysplasia	25 × 17 × 8	Clear (CE)	MOD (2 × 2)	Early invasive

O/E: on examination, IB: incisional biopsy, EB: laser excision biopsy, E: erythroplakia, L: leukoplakia, EL: erythroleukoplakia, WD: well-differentiated, MOD: moderately differentiated, CE: complete excision.

with cervical metastases. Improvements in survival and morbidity after treatment require early diagnosis and prompt intervention.

Oral precancerous lesions are clinicopathologically recognisable antecedents of invasive carcinoma that offer opportunities for therapeutic intervention during carcinogenesis.

In this study we examined a group of patients whose dysplastic oral precancerous lesions were diagnosed, managed, and followed up by one surgeon working to a standardised interventional laser surgical protocol that facilitates diagnosis and effective treatment.<sup>1,2</sup>

Fifteen of 169 patients with precancerous lesions (9%) had developed invasive carcinoma by the time of laser excision, but no distinct demographic or clinicopathological features helped to identify patients at risk preoperatively. Early identification of ‘unexpected’ oral SCC and its excision relies on intervention, and provides further evidence of the efficacy of carbon dioxide laser as the best tool for the management of potentially malignant oral lesions.

It remains unclear whether oral SCCs are always preceded by identifiable precancerous changes, but the finding of unexpected SCC in specimens of excised dysplastic lesions

supports the ‘progression’ model of carcinogenesis. The longest time interval between incisional biopsy and laser excision in this study was 6 weeks, which suggests that foci of oral SCC were present but missed at incision biopsy, presumably because of a sampling error.

In 54% of cases histological examination of incisional biopsy specimens was accurate in predicting what would be found on excision (Table 2), and these remain essential before excision of lesions, particularly to preserve tissue architecture and facilitate resection with appropriate margins.

Incisional biopsy specimens did, however, ‘underdiagnose’ the severity of dysplasia in an additional 48 cases (28%), in which dysplasia was more severe in the excised specimen than in the incisional biopsy specimen; this was particularly evident for mild and moderate dysplasia (Table 2).

Previous studies have suggested that interobserver variability by pathologists is responsible for differences in incision compared with excision biopsy grading,<sup>11–13</sup> but in our study the same team of specialist oral pathologists graded both incisional and excisional specimens. We think that the differences reflect the inadequacy of incisional biopsy specimens for the diagnosis of oral precancerous lesions.

While it has been suggested that multiple incisional biopsy specimens of large lesions and various visual aids may help in the examination and diagnosis of oral precancerous lesions,<sup>3,14</sup> we think that complete excision of the lesion remains essential, not only to establish diagnosis but also to facilitate early efficacious treatment of both dysplastic and early neoplastic lesions, particularly at a stage when oral SCC is clinically undetectable.

Multicentre, prospective, randomised, clinical trials are urgently needed to evaluate the role of interventional laser surgery further in the management of oral precancerous lesions and early invasive carcinoma.

### Conflict of interest

We have no proprietary, financial, professional or other personal interest of any nature or kind that could be construed as influencing the position presented in this manuscript.

### Acknowledgements

The authors wish to acknowledge the help of Professor Phil Sloan, Dr. Max Robinson and Dr. Atuora Okpokam of the Department of Pathology, and the Medical Physics Department at the Royal Victoria Infirmary, Newcastle upon Tyne without whom this study would not have been possible.

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