

Excision margins in squamous cell carcinoma of the tongue: A retrospective audit and review of the literature

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ABSTRACT

The incidence of close and involved tongue resection margins for squamous cell carcinoma (SCC) were reviewed with the aim to identify any possible need for change in the surgical approach to glossectomies. The histopathological reports of 101 partial glossectomies for SCC between 2006 and 2012 were retrospectively reviewed. Results: Overall 52 (51.5%) patients had one or more close or involved margin and 9 (8.9%) had both close and involved margins. 42 (41.5%) patients had close margins and 11 (10.9%) had involved margins. The inferior/lateral musculoalveolar margin was most frequently close/involved (32%) followed by deep margin (27%). The anterior margin was least close/involved (5%). The posterior and superior/medial margins were close/involved in 12% and 11% of cases respectively. Conclusions: 52.5% of patients had close or involved margins following surgery, potentially requiring further treatment to avoid an increased risk of tumour recurrence and the associated increase in morbidity and mortality. The inferior/lateral and deep margins were most frequently involved possibly due to the anatomical difficulties visualising and dissecting these margins. The potential explanations for these disparities and possible solutions are discussed.

Keywords: Squamous Cell Carcinoma; Tongue Cancer; Partial Glossectomy; Excision Margins

1. INTRODUCTION

The involvement of tumour at surgical margins after resection of squamous cell carcinoma from the tongue suggests a poor prognosis. Tumour margin involvement has an increased probability of local recurrence post glossectomy. The reported rates are 18% - 23.5% and the majority of recurrences occur within the first year of surgery [1-4]. Furthermore, the high rate of local tumour recur-

rence as a consequence of narrow margins may not decrease with the addition of adjuvant radiotherapy [5]. It is therefore not surprising that most studies show a negative impact of close or involved margins on disease-specific survival [1-3,6-10].

The impact of positive margins on local recurrence and survival highlights the need for adequate clearance margins during partial glossectomies. The current aim of surgical tumour excision is a microscopic margin of at least 5 mm, requiring an intraoperative margin of at least 1 cm [11]. However, the size of the margin taken is often limited by a number of different factors. Firstly, large margins may involve the sacrifice of a significant proportion of the tongue, floor of mouth or mandible, and this may cause a substantial impact on subsequent quality of life. The tongue is vital for both deglutition and speech, and removal of large areas of the tongue can result in the decreased ability to swallow and articulate. The size of the margin that can be taken is also influenced by the possibility of damaging surrounding anatomical structures. For example, the deep margin often lies close to the contralateral lingual artery, sacrifice of which may necessitate a nearly total glossectomy. Similarly the inferior/lateral margin may be limited by the mandibular periosteum meaning further margin clearance can only be achieved by some form of mandibulectomy. Surgeons performing glossectomies are therefore faced with the delicate task of balancing the need to achieve adequate tumour margins with the desire to retain function and quality of life and limit the cosmetic defect.

It is therefore important to gather information about the success of current surgical resection techniques for squamous cell carcinoma of the tongue in order to identify any need for change in the surgical approach to glossectomies. The aim of this study was to review the tumour margins following 101 consecutive partial glossectomies to assess whether sufficient margins are consistently being taken and, if not, whether particular margins are more commonly involved than others.

2. METHODS

The histopathology records of all patients with T1/T2 SCC of the tongue who underwent partial glossectomy at the John Radcliffe Hospital, Oxford between 2006 and 2012 were reviewed. One hundred and one patients were identified from the operating theatre log book and for these patients the superior/medial, inferior/lateral, anterior, posterior and deep/muscle margins were recorded. Data was retrieved from the patient's electronic case records and was taken from the reports independently of the surgical team and histopathologists. Any patients with tumour extending beyond the midline or to other anatomical structures or with dysplasia noted in the margins were excluded.

The UK guidelines, based on recommendations from the Royal College of Pathologists were used to define "clear", "close" and "involved" tumour margins. These guidelines define margins less than 1 mm (<1 mm) as involved, margins equal to 1 mm and up to 4.9 mm (≥ 1 mm to <5 mm) as close and margins of 5 mm or greater as clear (≥ 5 mm) [11].

3. RESULTS

Overall 42 patients (41.5%) had close margins and a further 11 (10.9%) had involved margins (**Table 1**). Some patients had more than 1 close or involved margin and 9 (8.9) patients had both close and involved margins. The inferior/lateral muscoal margin was the most frequently close or involved (32 of 101 [31.7%]) followed by deep margin (27 of 101 [26.7%]). The anterior margin was the least commonly close or involved (6 of 101 [5.9%]). The posterior and superior/medical margins were close or involved in 12 of 101 (11.9%) and 11 of 101 (10.9%) of cases respectively (**Table 2**).

Considering only the involved margins defined as <1 mm, the interior/lateral margin was still the most frequently affected with 6/101 (5.9%) involved, followed by the posterior margin (5/101 [5.0%]). The deep margin was involved in (3/101 [3.0%]) and the superior/medial and anterior margins were involved in 1/101 (1%) and 2/101 (2%) respectively.

4. DISCUSSION

In surgical excision of SCC of the tongue, the surgeon is often faced with a significant discrepancy between the tumour-free margins thought to be achieved *in-situ* and those reported from histopathological analysis. This is primarily due to tissue shrinkage, which occurs at various stages following the excision and processing of the tumour [12,13]. Mistry *et al.*, found that mean shrinkage of the tongue margins was 23.5%, with T1/2 tumours shrinking significantly more than T3/4 tumours [13]. Johnson *et al.*, reported average tongue mucosal margin

Table 1. Total number of patients with close, involved and close/involved margins.

Excision margin	Number of patients with margin involved
Close	42/101 (41.5%)
Involved	11/101 (10.9%)
Close or involved	52/101 (51.5%)
Close and involved	9/101 (8.9%)

shrinkage of 30.7% while the deep/muscle margin shrank by 34.5%, with the greatest proportion of shrinkage occurring immediately upon excision [12]. Therefore, most surgeons aim for an *in-situ* excision margin of 10 mm during glossectomies, in order to achieve histological clearance of 5 mm. Yuen *et al.*, advocate even wider excision margins, as the larger the area of macroscopically normal tissue around the tumour, the more likely it is that microscopic extensions are removed [14]. Alternatively, Kakarala *et al.*, suggest that the use of different types of surgical techniques can have an impact on the level of tissue distortion at the surgical margin, with steel scalpel causing the least margin disruption and harmonic scalpel creating less distortion than monopolar electrosurgery [15].

There is some evidence that the involvement of the deep margin in particular is related to increased rates of local recurrence of squamous cell carcinoma of the tongue [1]. Recurrence at this site is also more difficult to identify at an early stage during post treatment surveillance and more difficult to treat with further surgery, especially if the tongue has been reconstructed with free tissue transfer. It is therefore of note that in our audit, the deep margin was the second most frequently close/involved margin. There are a number of potential explanations for this high incidence of incompletely excised deep margins including the inability to visualise this margin, fear of damaging the contralateral lingual artery and a desire to maintain as much muscle as possible in order to preserve tongue function. It is also possible that this result is an artefact of the histological process as the deep margin has been shown to shrink by the greatest proportion [12]. The use of diathermy for tumour resection may also increase the incidence of "apparent" close margins, due to the destructive nature of this technique compared to cold steel excision, but this is likely to affect all margins equally. Diathermy excision with a Colorado needle was used in the majority of our cases.

The inferior/lateral margin was also commonly close or involved in our study. This may be because the margin often requires resection into the posterior floor of mouth or lingual alveolar mucosa making it more difficult to visualise and access compared to other margins. In some of these cases however, the lateral margin may actually

Table 2. Percentage of close, involved and close/involved cases for each margin.

Excision margin	Margin				
	Inferior/lateral	Superior/medial	Posterior	Anterior	Deep
Close	26/101 (25.7%)	10/101 (9.9%)	7/101 (6.9%)	4/101 (4.0%)	24/101 (24.0%)
Involved	6/101 (5.9%)	1/101 (1.0%)	5/101 (5.0%)	2/101 (2.0%)	3/101 (3.0%)
Close/Involved	32/101 (31.7%)	11/101 (10.9%)	12/101 (11.9%)	6/101 (5.9%)	27/101 (26.7%)

coincide with the mandibular periosteum. Such close margins may be considered “acceptable” as an uninvolved periosteum may act as a barrier, negating the need for mandibular resection in an effort to achieve at least 5 mm of clearance.

Many techniques have been used to try to reduce the frequency of close or involved margins. Firstly, a number of intra-operative measures have been developed in an attempt to achieve primary tumour clearance. Intra-operative frozen sections have traditionally been used for assessment of excision [16,17]. However, one margins found to be positive with frozen sections and subsequently rendered negative with further resection may still have an increased risk of local recurrence, especially if radiotherapy is not used postoperatively [18] and the use of frozen sections is therefore not popular in all units. Gauthier *et al.*, described a Mohs-like technique for excision of tongue SCC with a 1 - 5 mm margin and described no tumour recurrences, although their follow-up was short [19]. Intra-oral ultrasound for the assessment of tumour thickness and of intra-operative tumour clearance has also been used with some success [20,21]. The intra-operative use of Lugol’s iodine staining has also been reported to assist local clearance at the mucosal margins and reduce recurrence [22]. Kurita *et al.*, reported that intra-operative tissue staining and examination under a microscope permits visual inspection of a central section of the surgical specimen providing an accurate assessment and therefore better control of deep margins in oral cancer surgery [23]. Furthermore, Kee-reweer *et al.*, have recently used animal models to suggest that it may be possible to use intra-operative visualization techniques with near-infrared (NIR) fluorescence optical imaging to provide real-time image-guided surgery [24].

Further solutions to the problem of close margins could also include improved surgical techniques. Evidence for this comes from Lee *et al.*, who demonstrated a positive relationship between patient survival and surgeon caseloads. They suggested that the treatment strategies adopted by high-volume surgeons should be analysed and utilised more widely although it is unclear from this study whether the more experienced surgeons achieve a higher proportion of clear surgical margins [25]. Surgical techniques providing improved access

(such as mandibulotomy or pull through technique) and in continuity resection (where tongue, floor of mouth and neck specimen are removed en block) are employed by some surgeons to achieve better margin clearance, but evidence to support these is lacking. Others have noted that accurate and extensive imaging before surgery can reduce the frequency of involved margins [26,27].

In a cohort of 200 patients with oral SCC, Sutton *et al.*, reported close or involved surgical margins in 46.5% [4]. Interestingly, they found that these close or involved margins were highly related to histological indicators of aggressive disease such as lymphovascular and perineural invasion. They concluded that close surgical margins in oral SCC could be regarded as an indicator of aggressive disease and therefore surgical technique may not be the primary determinant of margins status.

The importance of distinguishing between close and involved margins has been emphasised by some [28,29]. In a retrospective review of 192 patients with oral and oropharyngeal cancer Wong *et al.* found that only involved margins were associated with local recurrence [29]. Overall, 12% of patients had involved and a further 55.7% had close (1 - 5 mm) margins. Sixty of the 107 patients with close margins received no adjuvant therapy, and of these only 5 had local recurrence. Close margins did have an adverse association with disease-free survival, however, the cut-off point was ≤ 1.6 mm, emphasising the arbitrary choice, by most researchers, of 5 mm as the cut-off point, and recommending redefining close margins as 1 - 2 mm.

Ultimately, even if there are tumour free margins at pathology, it is impossible to guarantee that there will be no recurrence. The microscopic presence of tumour cells within the margin is not the only predictor of recurrence and a number of other factors have been associated with increased rates of local recurrence including the histological pattern of invasion, site and stage of the tumour, perineural invasion and depth of invasion [1,17,30]. Methods of molecular and immunocytochemical detection of minimal residual cancer and field cancerisation have also been developed and may help identify patients at risk of developing loco-regional or distant recurrence [31].

However, careful surgery to achieve negative resection margins remains the most important factor in the effort to

improve local control of tongue cancer and disease-specific survival. Our results suggest that greater care needs to be taken, particularly at the deep/muscle and inferior/lateral margins, to ensure adequate resection. Certain access procedures and adjunct techniques such as intra-operative ultrasound may be of some help, but further studies are needed to demonstrate this.

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