

Clinical Paper  
Head and Neck Oncology

# Estimation of the width of free margin with a significant impact on local recurrence in surgical resection of oral squamous cell carcinoma

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S. Yamada, H. Kurita, T. Shimane, T. Kamata, S. Uehara, H. Tanaka, T. Yamamoto: Estimation of the width of free margin with a significant impact on local recurrence in surgical resection of oral squamous cell carcinoma. *Int. J. Oral Maxillofac. Surg.* 2016; 45: 147–152. © 2015 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

**Abstract.** The purpose of this study was to estimate the width of free margin with a significant impact on local recurrence in surgical resection of oral squamous cell carcinoma (OSCC). Clinical and pathological data of 127 consecutive patients who underwent radical resection of OSCC were analyzed retrospectively. The local control rate was compared between patients with clear, close, and involved surgical margins, changing the required width of free margin for the definition of ‘close surgical margin’ (from 1 to 5 mm). If a free margin of within 1, 2, or 4 mm was judged a close margin, the risk of local recurrence was significantly different among the patients with clear, close, and involved surgical margins. If the definition of close margin was within 5 mm of the resection margin, the difference between clear and close margin did not reach statistical significance. The results of this study suggest that 5 mm of clearance at the surgical resection margin should be the index of oncological surgery. More than 5 mm of histological free margin around OSCC is not justified in terms of the risk management of local recurrence and the resultant morbidity.

**Key words:** surgical margin; free margin; margin clearance; close margin; involved margin; surgical resection; tumour clearance; local recurrence.

Accepted for publication 30 September 2015  
Available online 27 October 2015

The fundamental goal in curative oncological surgery is to completely resect the malignant tumour and to leave no residual viable tumour cells. Surgical resection of the primary cancer with adequate margins

is an essential component in the treatment of patients with oral squamous cell carcinoma (OSCC). Margin status is one of the most important predictors of the prognosis. It has been suggested that failure to

achieve a clear surgical margin results in an increased risk of local recurrence and subsequently a poor prognosis.<sup>1–11</sup>

Successful surgical resection of the primary site requires a margin of uninvolved

tissue around the primary neoplasms ('free margin') in a pathological assessment of the surgical specimens. Some investigators currently require 5 mm or more healthy tissue around the tumour to declare a clear surgical resection in the pathological assessment,<sup>1,2,5,12</sup> while others consider that less free normal tissue (e.g. 2 or 3 mm) indicates adequate resection.<sup>6-8</sup> There is a lack of consistency regarding the amount of free margin required to interpret the radical resection of OSCC as complete, because no study has precisely examined the width of free margin for the definition of 'close surgical margin' (from 1 to 5 mm).<sup>1,2,5-8,12</sup> The purpose of this study was to estimate the width of free margin that has a significant impact on local recurrence of OSCC.

## Materials and methods

A historical cohort of 148 consecutive patients (1990–2007) who underwent a planned radical resection of their primary OSCC with or without adjunctive radiotherapy and/or chemotherapy, for previously untreated OSCC, was examined. Of these patients, those with T4b tumours ( $n = 8$ ) were excluded from the study because of an uncertainty in defining the surgical margin (i.e., invasive front in the masticatory space). Patients who had dysplastic epithelium at the mucosal margin ( $n = 13$ ) were also excluded, because the presence of dysplastic epithelium at the surgical margin is of grave biological significance. Consequently, 127 patients were available for the study.

Pathology reports on surgical specimens were reviewed for the status and the minimum width of free margin. A resection margin with evidence of carcinoma, including carcinoma in situ, was considered an involved margin. The minimum width of tumour-free tissue around the tumour in either mucosal or deep margins was recorded to the nearest millimetre (1, 2, 3, 4, 5, and >5 mm). Conventional microscopic processing was used to assess the margins of the surgical specimen. Representative vertical sections were obtained at 2- to 5-mm intervals throughout the specimen using the bread-loaf and additional quadrant method. Surgical specimens that included hard tissue were processed after demineralization. An experienced pathologist and the surgeon responsible assessed all histological sections.

The primary endpoint was the local control rate. The time to primary local recurrence was calculated using the Kaplan–Meier actuarial method.<sup>13</sup> Calcula-

tion was started at the time of the patient's first visit. The presence of histopathologically proven malignant lesions adjacent to the resected primary site was considered uncensored observation. Indistinguishable concurrent local and regional recurrence was considered uncensored observation. Second primary SCC was defined as SCC arising at a different site distinctly separate from the resected primary site, at a distance of more than 2 cm, and was considered censored observation. Multivariate Cox proportional hazard models<sup>14</sup> were used to test the hypothesis of an increased hazard of local recurrence after controlling for potentially confounding variables (primary site, T-classification,<sup>15</sup> degree of differentiation,<sup>16</sup> mode of invasion,<sup>17</sup> preoperative treatment, and postoperative radiotherapy). The risk of local recurrence was compared between the patients with clear surgical margins and those with close margins, altering the width of free margin required for the definition of a close margin. Analyses were performed using StatView software package for Macintosh (SAS Institute, Inc., NC, USA). All  $P$ -values of <0.05 were considered significant.

This study was approved by the committee on medical research of the study university.

## Results

Patient characteristics are summarized in Table 1. Eighty-two patients underwent preoperative chemotherapy and/or radiotherapy. Thirty-five patients underwent postoperative radiotherapy over 50 Gy within 6 weeks after surgery due to the presence of indication criteria, including a close or involved surgical margin, multiple lymph node metastases, or extracapsular spread of lymph node metastasis. Of the 127 patients, 10 (7.9%) had an involved margin, 24 (18.9%) had a minimum width of free margin  $\leq 5$  mm (within 5 mm), and 93 (73.2%) had a free margin of >5 mm. By chance, there was no patient who had a minimum width of free margin between 2 and 3 mm. The median duration of follow-up was 43.0 months, ranging from 2 to 180 months. Seventeen patients developed local recurrence and nine patients had regional (lymph node) recurrence. Distinguishing between local and regional recurrence was not particularly difficult. There was no patient with second primary SCC.

A comparison of local control curves among the involved, close, and clear margins, drawn with different definitions of a close margin, is shown in Fig. 1 (A: within

Table 1. Clinical and pathological characteristics of the patients.

Characteristics	
Sex, female/male	54/73
Age, years, median (range)	66.0 (27–84)
Primary site	
Tongue	59
Lower gum	21
Upper gum	16
Cheek mucosa	16
Floor of mouth	14
Hard palate	1
T-classification	
T1	20
T2	39
T3	22
T4a	46
N-classification	
N0	72
N1	20
N2b	26
N2c	8
N3	1
Clinical stage	
I	18
II	26
III	20
IV	63
Degree of differentiation	
Micro-invasive	4
Well-differentiated	79
Moderately differentiated	38
Poorly differentiated	6
Mode of invasion	
YK-2	18
YK-3	55
YK-4C	41
YK-4D	13
Preoperative therapy	
Yes	82
No	45
Postoperative radiotherapy over 50 Gy	
Yes	35
No	92
Follow-up period, months, median (range)	43.0 (2–180)
Width of free margin	
Involved	10
0 to $\leq 1$ mm	6
> 1 to $\leq 2$ mm	8
> 2 to $\leq 3$ mm	0
> 3 to $\leq 4$ mm	5
> 4 to $\leq 5$ mm	5
>5 mm	93

5 mm, B: within 4 mm, C: within 2 mm, D: within 1 mm). The status of the surgical margin significantly influenced local control in the univariate analyses (log-rank test,  $P < 0.05$ ). There was a statistically significant difference in the local control rate among the patients with involved, close, and clear margins for all curves. However, the difference between the patients with close margins and those with clear margins was relatively weak if the tumour definition of a close margin was

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