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The Impact of Frozen Sections on Surgical Margins in Squamous Cell Carcinoma of the Oral Cavity and Lips: A Retrospective Analysis 1998 – 2008

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Abstract

Objectives. Using intraoperative frozen sections for margin assessment is widely done by head and neck surgeons. The objective of this study was to evaluate the impact of frozen sections on different grades of surgical margin status in the permanent section of squamous cell carcinoma of the oral cavity and lips.

Materials and Methods. A retrospective study was performed of 178 patients with squamous cell carcinoma of the oral cavity and lips, who were treated surgically with the intention of curative resection. Frozen sections, pT-stage, grading, and tumor localization were compared by uni- and multivariate analysis in patients with positive, intermediate, and negative surgical margin status. Special attention was given to the relationships among the following factors: tumor site, different grades of intraoperative frozen sections, and positive or intermediate margins.

Results. Performed on 111 patients (62.4%), intraoperative frozen sections did not have any statistically significant influence on margin status, independent of whether the surgical margin was positive (involved by carcinoma) (p=0.40), intermediate (involved by dysplasia or carcinoma in situ) (p=0.70), or negative (clear of any histopathological changes) (p=0.70). In 44.4% of all patients, frozen sections were taken from the same area where the margin was classified as positive or intermediate. Surgical margins involved by carcinoma were encountered in 23% of all the patients and were significantly associated with pT4-tumors (OR 5.61, p=0.001). The chance for negative margins in permanent sections was significantly higher in tumors located in the tongue (OR 4.70, p=0.01).

Conclusions. The use of intraoperative frozen sections in squamous cell carcinoma of the oral cavity and lips does not have any significant impact on surgical margin status and should, therefore, not routinely be done. In addition, head and neck surgeons should be aware that negative frozen sections may not guarantee tumor-free surgical margins even if taken from the same area.

Introduction

Around 260 patients in Switzerland die every year from cancer of the oral cavity and pharynx[1]. Besides radio- and chemotherapy, surgical removal of the tumor is the main treatment strategy for most of these patients. Various factors exist that affect the prognosis of oral squamous cell carcinoma (SCC). Apart from extracapsular spread in tumors with lymph node metastasis, one of the main prognostic factors is the surgical margin status[2].

Although no consensus exists about what constitutes a "positive" surgical margin, it is widely accepted that tumors at the inked resection margin are associated with lower survival rates [3-7]. Therefore the surgeon`s primary aim is to achieve a clear surgical margin and most, but not all [8-9], centers follow this practice.

Frozen sections may be performed before the tumor is excised, from the surgical bed and/or from the surgical specimen. From sampling technique to microscopic assessment, many biases may be introduced during this procedure. Furthermore, frozen section analysis costs USD $3,123 on average per patient with an estimated cost-benefit ratio of 20:1[10]. Therefore, and because of increasing costs in the healthcare system, the diagnostic value of frozen sections in head and neck oncological surgery was investigated recently. The impact of frozen sections on survival and local recurrence is still controversial[11-12]. However, two studies including the same patient population[7, 13] showed no effect of frozen sections on involved surgical margins, and Ribeiro et al. stated no effect on close surgical margins[14]. So far there is no evidence of an association of frozen sections with premalignant changes in the surgical margin of permanent slides.

The aim of this study was to investigate whether frozen section analysis undertaken during surgery had any effect on different categories of surgical margins, including carcinoma in situ and dysplasia in the margin of oral/lip squamous cell carcinoma.

Materials and Methods

Selection of surgical cases

Between 1998 and 2008, 374 patients with head and neck cancer were treated at the Department of Craniomaxillofacial and Oral Surgery at the University Hospital of Zürich, Switzerland. Inclusion criteria for our study were as follows: (i) patient had SCC of the oral cavity or upper/lower lips; (ii) no previous surgical excision had been performed for this tumor; and (iii) the operation was done with curative intent. Overall 196 patients had to be excluded with 63 patients showing another type of tumor. Other reasons for exclusion were other localization of the tumor, palliative surgery, patients already surgically treated before, missing charts with detailed clinical and pathological information and if only dysplasia was seen in permanent histological section when initially a squamous cell carcinoma was anticipated. Finally, 178 patients were included in the retrospective analysis.

Data collection and definitions

A standardized Excel-chart was developed to assess pathological and clinical parameters. Data were obtained from pathology reports and patient charts, which were assessed by a single observer (S.G.). Throughout the study period, queries were resolved through discussion with the senior researcher (A.K).

Clinical variables evaluated included gender, age, tumor localization, and different surgical procedures. The pathological variables examined comprised pT-stage, histologic grading 1-3, histologic subtype of squamous cell carcinoma, and special characteristics of tumors like necrotic section, ulceration, and bone invasion. We further analyzed the margin status and the distance from tumor to resection margin, as well as whether or not intraoperative frozen sections for margin evaluation had been performed. No distinction was made between mucosal, deep, or bone resection margins. The decision about performing frozen sections was left to the surgeons' judgment. If frozen sections were performed, any area that was regarded as suspicious by the surgeon was sampled. The frozen and permanent sections were evaluated by different experienced histopathologists. Further, we divided the histopathological margins of permanent sections into three categories:

1) "Positive" margins: Involved by invasive carcinoma (incl. perineural invasion within the margin).
2) "Intermediate" margins: Involved by carcinoma in situ and/or low to high grade dysplasia without invasive carcinoma in the margin.
3) "Negative" margins: No involvement by invasive carcinoma, carcinoma in situ, or dysplasia.

Special attention was paid to premalignant changes in surgical margins; therefore, as proposed by Batsaki,[15] dysplasia and carcinoma in situ were not included in the definition of "positive" margins. In cases with intermediate or negative margins, the minimal distance from tumor to resection margin was recorded and divided into three categories (i) <1mm; (ii) 1-5mm; and (iii) >5mm. All cases with positive or intermediate margins in the permanent histological slides were examined to see if the frozen sections showed infiltration with carcinoma (positive frozen section), dysplasia and/or carcinoma in situ (intermediate frozen section), or if they were clear of any pathological changes (negative frozen section). Furthermore, it was noted if frozen sections were performed on the same area where the histopathological changes in the permanent slide were seen. If the surgical margin was involved by invasive carcinoma, the largest tumor-diameter was measured to define the pT-stage. In 28 cases data concerning the pT-stage and in 3 cases data about the minimal distance from tumor to resection margin were missing in the pathology report. A senior pathologist (C.G.) and the first author (S.G.) reviewed the permanent slides of these 31 cases for the missing data.

Tumor localization was defined as the site where the major part of the tumor was located. When the larger part of the tumor, e.g., mainly affected the floor of mouth, the tumor was considered as floor-of-mouth cancer. In assessing different surgical procedures, it was sometimes difficult to divide operations into different categories. Therefore in our study tongue and floor-of-mouth resection, and hemimaxillectomy and upper jaw alveolar resection were considered to be one category each. The category of lower jaw resection included mandibular rim resections and segmental block resection as well. In 6 cases two surgical procedures were reported.

Data management and statistical analysis

Data were coded in Excel and analyzed with the SPSS-PC package Version 17.0 using chi-squared tests for binary variables. As a baseline for regression analyses, variables were chosen on the basis of most data observed (pT1 for pT-stage, lower jaw for tumor localization, and local resection for operations) or on the basis of pathological parameters (G1 for grading). Results of the statistical analysis with p-values smaller than 5% were considered to be statistically significant. Values bigger than 5%, but smaller than 10%, were interpreted as tendencies.

Results

A total of 178 patients were reviewed in this retrospective analysis. The series comprised 102 males (57.3%) and 76 females (42.7%). The mean age was 63.5 years (age range from 32 to 89) (Figure 1). The site distribution is summarized in Table 1, with the lower jaw being the most common site encountered in 47 patients (26.4%). Other locations were noted in 14 patients (7.9%), including the buccal mucosa or palato-glossal fold. Other tumor locations were the tongue in 39 (21.9%), the floor of the mouth in 34 (19.1%), the upper jaw in 29 (16.3%) and the upper and lower lips in 15 patients (8.4%).

Tumor staging was as follows: pT1 in 83 (46.6%), pT2 in 53 (29.8%), pT3 in 10 (5.6%), and pT4 in 32 (18%) patients. Twenty-eight patients were identified with grade 1 histology (15.7%), 108 with grade 2 (60.7%) and 42 with grade 3 (23.6%). Surgical procedures performed included lower jaw resection in 47 (26.4%), floor-of-mouth and tongue resection in 34 (19.1%), hemimaxillectomy and alveolar resection of the upper jaw in 27 patients (15.2%), and other resections, like lip resection, in 8 (4.5%) patients. In 68 patients (38.2%), a local excision was done, including CO2-laser excisions. In 6 out of 178 patients (3.4%), two surgical procedures were reported during the same operation.

Frozen sections

Intraoperative frozen sections to assess surgical margin status were performed on 111 of 178 patients (62.4%), depending on the operating surgeon's practice preference (Table 1).

Positive resection margin in patients with frozen sections occurred in 22 of 111 tumors (19.8%). This was not significantly lower than in patients without frozen sections, with 19 positive margins in 67 patients (28.4%, OR 0.70, p=0.40). Intermediate margins occurred more often when frozen section analysis was undertaken (12.6% vs. 7.5%, OR 1.26, p=0.70). Similar results could be found for negative resection margins with an odds ratio of 1.15

(67.7% vs. 64.2%, p=0.70). However no statistical significance was observed in any of the 3 categories. Therefore, in our multivariate logistic regression analysis, the practice of using frozen sections for achieving negative margins was not significantly associated with the margin status of permanent histological slides, independent of positive (p=0.40), intermediate (p=0.70), or negative (p=0.70) surgical margin (Table 2). Univariate analysis confirmed these results.

The proportion of frozen sections performed ranges from 15 of 32 cases (46.9%) in pT4- tumors to 8 of 10 cases (80%) in pT3-tumors and a multivariate logistic regression analysis confirmed that frozen sections were significantly more often taken from pT2-tumors (OR 2.53, p=0.03) compared to pT1-tumors. Grading and tumor localization did not seem to have any statistically significant influence on the decision to take frozen sections (Table 3).

To focus on tumors with positive or intermediate surgical margins, frozen sections were more frequently performed on cases with intermediate than with positive margins (53.7% vs. 73.7%) (Table 4). In 22 of 41 patients with positive surgical margins, intra-operative frozen section analysis was undertaken (53.7%). Ten out of these 22 patients (45.5%) had frozen sections with invasive carcinoma or dysplasia. In one half of these 10 cases, re-resection was performed at the same site until the frozen sections were negative. In the other half, no further frozen sections were taken, and the tumor was excised with a wide margin at this crucial site. However, in all of the 10 cases with invasive carcinoma or dysplasia in the frozen sections and positive surgical margins, the sites from which frozen sections were taken and the areas where the surgical margin was positive were not identical. In 5 of the other 12 patients, frozen sections were performed on the same site where the surgical margin was positive, which accounts for 22.7% of all patients with positive surgical margin and frozen sections.

In 14 out of 19 patients (73.7%) with intermediate surgical margin status, frozen sections were performed. Half of these patients showed positive or intermediate frozen sections; in one patient, the frozen section was performed a second time until a negative result was achieved; and in the other 6 cases, tumors were excised with a wider margin, without a second frozen section analysis undertaken. However, in 5 of these 6 tumors, intermediate surgical margins were reported as being located at the same site as the frozen section. In 11 of 14 patients (76.8%), frozen sections were located at the same site where the intermediate surgical margin showed dysplasia/carcinoma in situ. Overall, in 16 out of 36 patients (44.4%) with frozen sections and positive or intermediate margins, the location was identical according to the pathology report.

Surgical margin status

In 41 of 178 patients (23%), the histological margins of the permanent slides were involved with invasive carcinoma and were considered to be positive. Nineteen patients (10.7%) showed either carcinoma in situ (1 patient) or dysplasia (18 patients) in the surgical margin and were considered to have intermediate margins for data analysis. One of these 19 patients had carcinoma in situ in the margin, and half of the remaining 18 tumors with intermediate margins were classified as low/middle grade and high grade dysplasia, respectively. However, the majority of patients had negative surgical margins (118 patients, 66.3%) (Table 1).

The association of surgical margin status with different factors makes the use of multivariate models reasonable. As mentioned above, frozen sections showed no significant influence on surgical margin status. However, the chance of a positive surgical margin is significantly increased by the factor 5 in pT4-stage tumors compared to pT1-tumors (OR 5.61, $p=0,001$). Showing the same tendency are pT3-stage tumors (OR 4.44, $p=0,055$) (Table 2). Consequently, histologically proven bone invasion, which was reported in 23 of 178 cases (12.9%), showed a significant correlation to positive surgical margins in permanent slides (OR 4.47, $p<0.001$). Figure 2 demonstrates the increasing ratio of positive margins with increasing pT-stage, and the inverse correlation with negative surgical margins. Regarding the tumor site, the tongue is rarely associated with positive surgical margins (OR 0.21, p=0,03); consequently, tumors located at this site have a 4.7-fold increased chance of a negative surgical margin (OR 4.70, p=0.01) (Table 2). This could be confirmed in a univariate logistic regression analysis demonstrating significantly more frequent negative surgical margins after floor-of-mouth resection, including tongue resection, compared to local resection (OR 4.19, p=0.01). In addition, floor- of-mouth and tongue resection (OR 0.17, p=0.09) and hemimaxillectomy including upper alveolar resection (OR 0.14, p=0.06) both tend to be associated with intermediate surgical margins in permanent slides (Table 5).

Ulcerated tumors were encountered in 30 cases (16.9%). Subtypes of squamous cell carcinoma were not consistently reported, and no further analysis was performed.

Distance from tumor to resection margin

Out of 137 surgical specimens with intermediate or negative margin status in permanent slides, 110 tumors (80.3%) were located at least 1 mm away from the surgical margin with a distance between 1 and 5 mm most often reported (in 86 of 137 cases, 62.8%) (Table 1).

The distance from tumor to resection margin is significantly influenced by pT-stage (pT2 p=0.03, pT3 p=0.01, pT4 p<0.001) and by tumors located in the tongue (p=0.01). At this site, 22 of 39 tumors (56.4%) were located within 1-5 mm from the margin and only 3 surgical specimens (7.7%) showed infiltration of the margin by invasive carcinoma. Figure 3 demonstrates the correlation of pT-stage with distance from tumor to resection margin. With increasing distance to surgical margin, the proportion of pT1-tumors increases from 24.4% with positive margins to 70.8% with a clear margin of more than 5 mm. The inverse correlation is illustrated for pT4-tumors with a decrease from 41.5% to 4.2%. In only 10 patients were pT3-tumors encountered; therefore, no clear statement concerning the distance could be made, and no multinominal logistic regression analysis was performed.

Discussion

All together 178 patients were studied, presenting with squamous cell carcinoma of the oral cavity or lips between 1998 and 2008, who were surgically treated with a curative intention. In 111 (62.5%) patients, intra-operative frozen sections for margin evaluation were performed. The practice of taking frozen sections did not have any statistically significant influence on the margin status of the surgical specimen, irrespective of whether the margin was involved by invasive carcinoma or by dysplasia/carcinoma in situ. Furthermore, the data support that frozen sections may be negative, although taken from the same area where the surgical margin was classified as positive or intermediate. However, surgical margin status was significantly associated with two factors: tumor localization and pT-stage. Tumors located in the tongue led more often to negative margins, and pT4-tumors had 5 times as many positive margins as pT1-tumors. In negative or intermediate surgical margins, the distance from tumor to resection margin increased with pT-stage and showed a significant correlation to tumors located in the tongue.

The influence of frozen sections on surgical margin status had not been assessed until lately. This topic was addressed by two authors investigating the same patient population[7,13]. Binahmed et al.[7] examined the clinical significance of positive surgical margins in a cohort of 425 patients with oral squamous cell carcinoma. The diagnosis was biopsy-proven, and patients had been previously untreated. Intraoperative frozen sections, performed on 52.9% of the patients, were associated neither with involved nor with clear margins. However, there are no p-values available in this paper, and it is not clear if uni- or multivariate analysis was used. Similar results were published by Nason et al.[13], who investigated the same patient cohort as Binahmed et al[7]. They performed a subgroup-analysis with a remaining cohort of 277 patients, recording the width of the clear margin. Both studies classified surgical margins as "positive" if they were involved with invasive carcinoma.

Surgical margins with carcinoma in situ or dysplasia were not assessed in these studies. Our study confirms these results. We could not find any significant association of frozen sections and margin status, independent of whether the margin was positive, intermediate, or negative. The association between frozen sections and surgical margins with carcinoma in situ or dysplasia has not been assessed so far.

Byers et al.[16] reviewed 216 patients with SCC of the head and neck, who underwent surgical treatment including frozen section analysis. Of these tumors, 67% were adequately excised through the surgeon's judgment without taking frozen sections. This figure raises the question about the diagnostic value of frozen sections in general. In the current study, in 36 of 60 patients (60%), positive or intermediate surgical margins went undetected in spite of using frozen sections; therefore they did not benefit from this practice. In more recent studies this figure for undetected positive surgical margins ranges between 15.4% and 83.3%[10,12,17-18], and these results were confirmed by the 60% of patients in our study cohort. However, a comparison of these results is difficult. Definitions of "positive margin" were different in all studies; tumor site was not consistent; and other tumor types were included in some instances: Di Nardo et al.[10], for example, included all head and neck malignancies, with 13.75% of tumors being non-squamous cell carcinoma, and only 28% of tumors were located in the oral cavity. Ribeiro et al.[14] reported on the resection of oro-pharyngeal carcinoma in 82 patients. In 12 of the 82 patients, surgical margins were positive for invasive carcinoma, and 10 of these patients had negative frozen sections (83.3%).

According to pathology reports, in only 16 of the 36 patients (44.4%), frozen sections were located in the same area where the surgical margin showed pathological changes. This finding demonstrates one of the main limitations of frozen sections: the sampling. Although surgeons try to take frozen sections from the crucial sites, sampling error is the most frequent cause of error in using intraoperative frozen sections[8,19]. Tumors are 3-dimensional structures, and it is not practicable to evaluate the whole surgical margin by means of frozen sections[3].

This highlights the importance of sampling the crucial sites from which frozen sections should be taken. So far no reliable test exists to detect in-vivo where the tumor front is located.

After an initially positive frozen section, a second frozen section was done in 3 of 17 patients (17.6%) until it was negative. In one of these 3 patients, we found dysplasia in the margin of the permanent section at the same site. The procedure of doing multiple frozen sections at the same site leads to another source of bias: the relocation by the surgeon. It takes about 30 minutes for the pathologist to process a sample of frozen section. During this time the surgeon continues with the operation. As soon as the surgeon gets a positive histopathological result, he has to relocate the exact position of the former frozen.. Kerawala et al.[20] showed that the mean error in relocating the site of frozen sections in oropharyngeal cancer is 9 mm for samples at the mucosal margin and 12 mm for samples placed deep into the tumor. Even if no further frozen section is performed and tumor excision is done with a wider margin at the crucial site, the problem of relocation persists.

In the present study, the decision about the site from which the frozen sections should be taken was left to the surgeons' judgment and was not assessed in the study. Currently no standard protocol exists for intraoperative margin analysis in patients with head and neck carcinoma, although the practice of undertaking frozen section is widely used in head and neck oncology surgery. Meier, Oliver, and Varvares[9] found, in their survey of 1500 members of the International American Head and Neck Society, that 97% use frozen sections for margin evaluation in the oral cavity and pharynx, with 76% taking those from the surgical bed and 14% from the resected surgical specimen. Methods may vary between or even within institutions. In a 2-question survey from Black et al.[21] that included responses from 100 medical centers, 32% of pathologists stated that more than one method of frozen section practice was in use in their institutions. Most pathologists (67%) receive multiple small pieces of tissue for frozen section analysis, and one-third receive the entire specimen for intraoperative margin analysis. However, no explicit evidence exists on whether frozen sections should be taken at the surgical bed or from a specimen[9,18].

Positive surgical margins, one of the most important prognostic factors[2], are 1.7 times more likely to be encountered in oral carcinoma than in other head and neck tumors[3]. In the present study, 23% of all the patients had a positive surgical margin in permanent sections. This finding is similar to the results of other studies that reported ratios between 4.5% and 52.9%[3-7, 12-14, 18, 22-23]. To what extent these figures represent the aggressive behavior of the tumors rather than inadequate surgical resection, as proposed by Sutton et al.[5], is still a matter of research. However, the result does not support the mentioned hypothesis, as we could not find any statistically significant influence of histological grading on positive surgical margin status.

Tumors from the tongue were associated more frequently with negative surgical margin status in our study, a fact that has been reported before[22]. This may be explained by the fact that the circumference of the tumor is easily palpable and that less anatomical limits are given which leads to a better access to the tumor site by the surgeon.

The present study has a number of limitations. It did not differentiate between patients with and without prior radiotherapy. Preoperative radiotherapy is often associated with extensive fibrosis and inflammatory reaction, which makes the histological assessment of frozen sections [17] and the total resection even more difficult. What is more, we lacked the resources to microscopically review all frozen sections in order to look for false-positive and false-negative results. Compared to formalin fixed tissue, cellular morphology may not be clearly defined, and diagnosis of frozen sections has to be made under time pressure. This can lead to interpretational difficulties. It is worth noting that the accuracy of frozen sections was previously reported to be over 98%[10,14]. Therefore the lack of detailed review may not have had any significant impact on our results. In our study not all squamous cell carcinomas were biopsy-proven before radical surgery. However, every surgical procedure, including excision-biopsy, was intended to remove the lesion in toto with a safe margin of 1 cm, if allowed by vital anatomic structures in the neighborhood. Dysplasia in surgical margins was classified as a separate group, although Abbey et al.[24] found that reproducible agreement among oral pathologists concerning the diagnosis of "dysplasia" was only 81.5%. This may distort our findings.

In conclusion, the oral cavity is a complex 3-dimensional anatomic region and a wide variety of vital structures are located very near. Therefore tumors located in this area make great demands on the surgeon aiming for total tumor excision. The practice of intra-operative frozen sections is one of the main tools used to reach this target. However, our results show that the diagnostic value of intraoperative frozen sections for margin assessment in squamous cell carcinoma of the oral cavity and lips is limited. There was no impact of frozen sections on margins involved by carcinoma or by other pathological changes, such as dysplasia or carcinoma in situ. Furthermore, it was shown that frozen sections, which represent only a small part of the whole surgical margin, may be negative, even if taken from the same area where the surgical margin is positive. This highlights the fact that frozen sections are only as good as the sampling is[14].

The practice of routinely doing frozen sections in squamous cell carcinoma of the oral cavity and the lips is questionable. It does not seem to significantly influence the outcome of surgical margin status and in some situations it may even mislead the surgeon. The necessity of frozen sections should be evaluated case by case. The specific situations in which frozen sections are necessary and what is the most useful sampling protocol may be the subject of further research agenda.

Figure 1: Distribution of age among 178 patients with squamous cell carcinoma of the oral cavity and lips

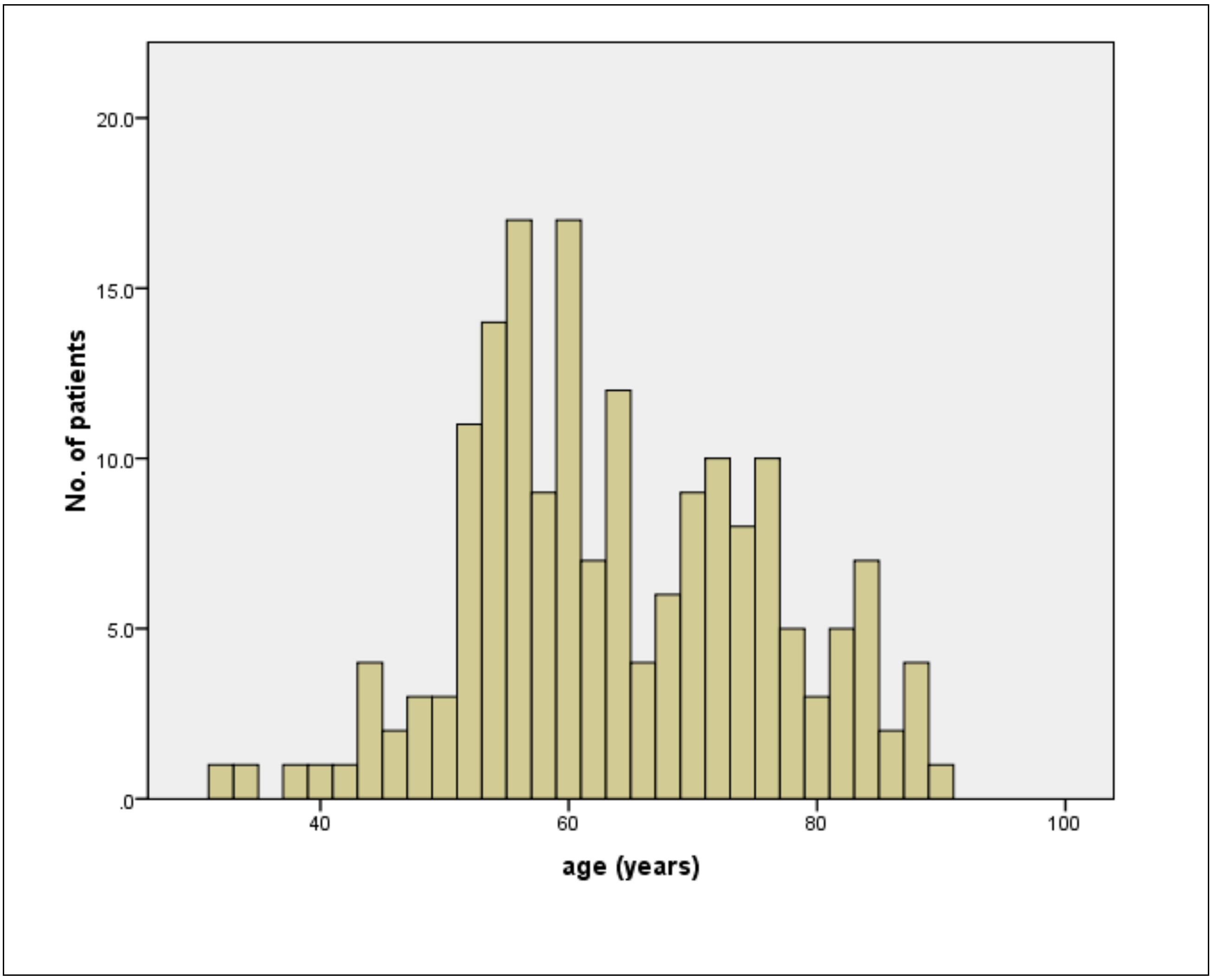

Figure 2: Margin status in relation to pT-stage

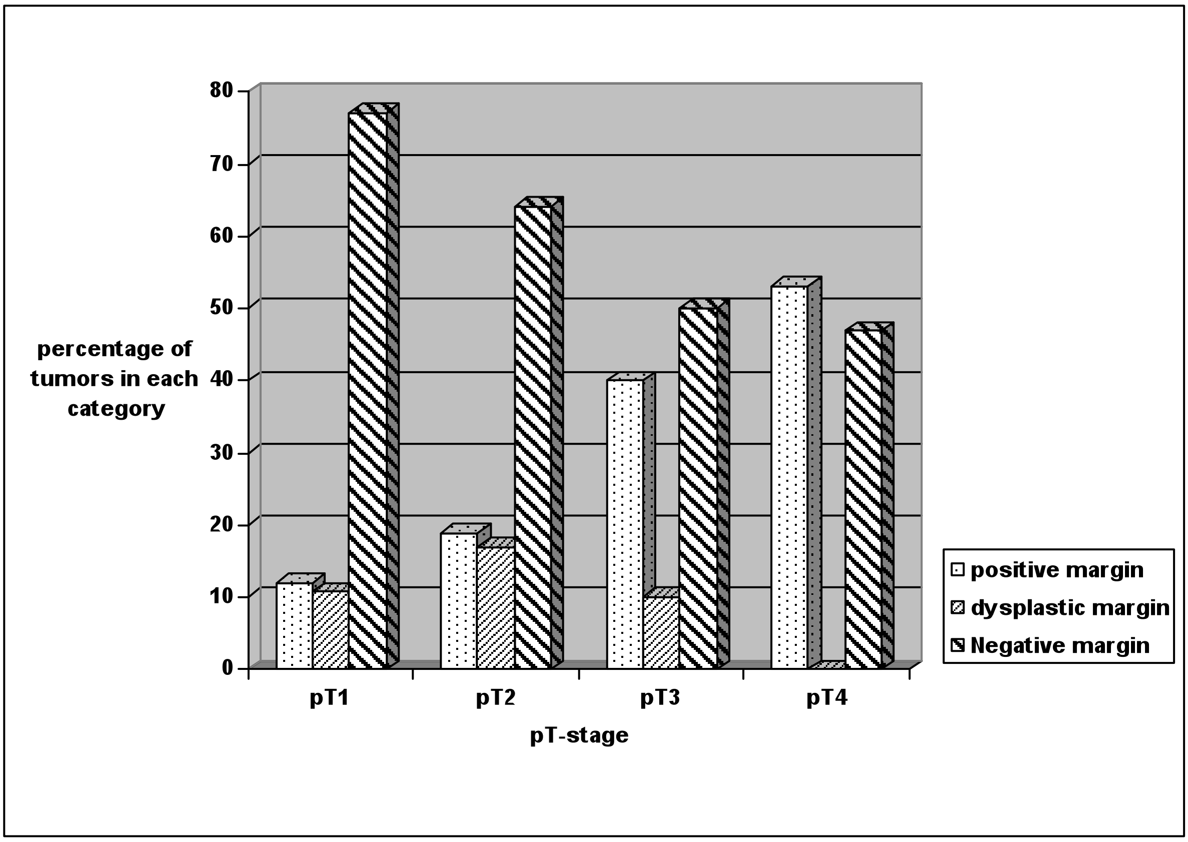

Figure 3: Distance [mm] from carcinoma to surgical margin according to pT-stage.

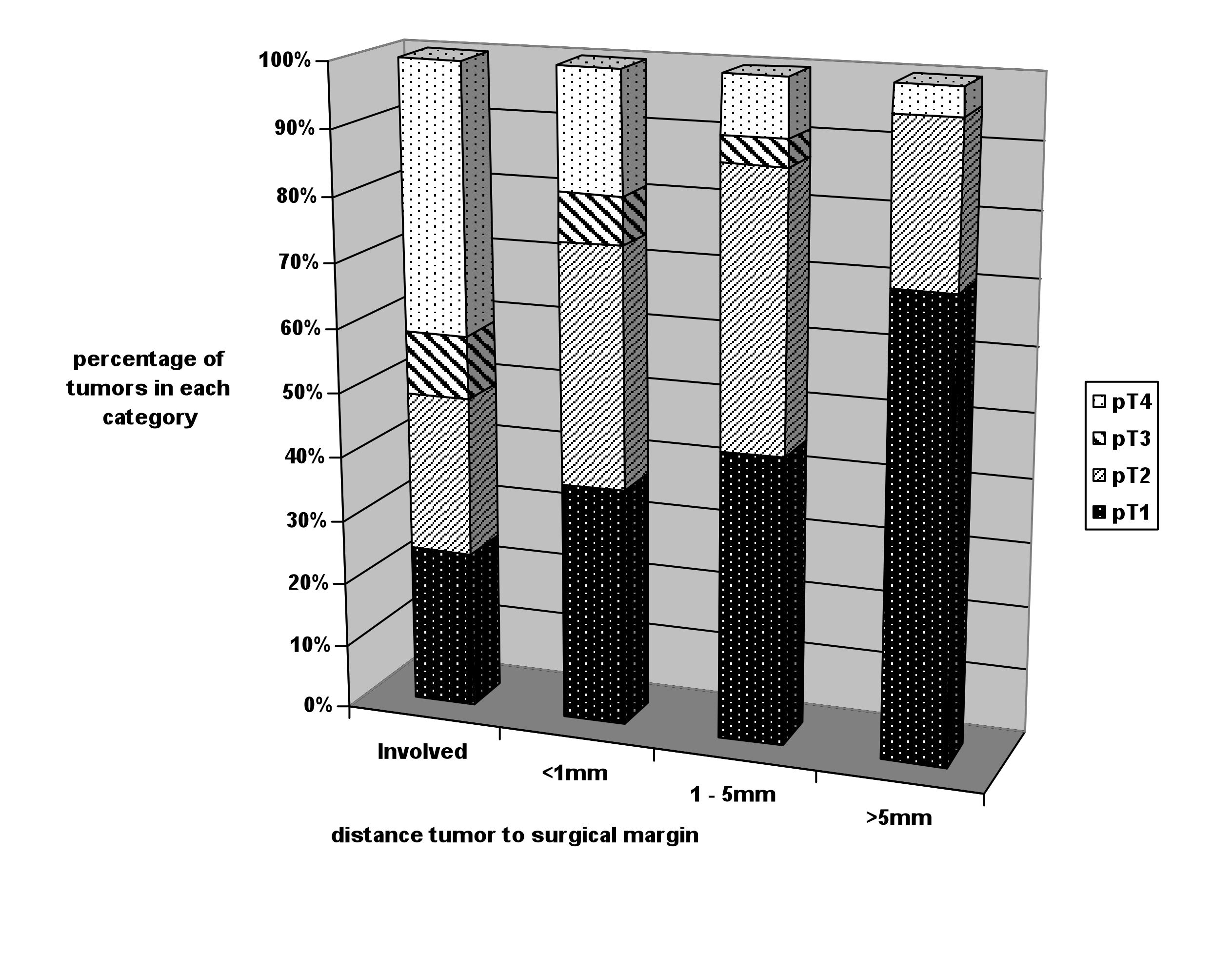

Table 1: Characteristics of 178 patients with squamous cell carcinoma of the oral cavity between 1998 – 2008

	No of Cases	%
Patients		
Men	102	(57.3)
Women	76	(42.7)
Mean Age	63.5 years	(range 32-89)
Tumour localisation		
Lower jaw	47	(26.4)
Tongue	39	(21.9)
Floor of mouth	34	(19.1)
Upper jaw	29	(16.3)
Upper and lower lips	15	(8.4)
Other locations	14	(7.9)
pT-Stage		
pT1	83	(46.6)
pT2	53	(29.8)
pT3	10	(5.6)
pT4	32	(18.0)
Grading		
G1	28	(15.7)
G2	108	(60.7)
G3	42	(23.6)
Special features of tumours		
Necrotic	1	(0.6)
Ulceration	30	(16.9)
Bone invasion	23	(12.9)
Surgical procedures ¥		
Local resection	68	(38.2)
Lower jaw resection	47	(26.4)
Floor of mouth/Tongue resection	34	(19.1)
Hemimaxillectomy/Upper jaw alveolar resection	27	(15.2)
Lips and other resections	8	(4.5)
Surgical Margins status		
Positive margin (involved by carcinoma)	41	(23.0)
Intermediate margin	19	(10.7)
- Carcinoma in situ	1	(0.5)
- low/middle grade dysplasia	9	(5.1)
- high grade dysplasia	9	(5.1)
Negative margin	118	(66.3)
Distance carcinoma – resection margin	137	(77.0)
- <1mm	27	(15.2)
- 1 – 5 mm	86	(48.3)
- > 5mm	24	(13.5)
Frozen sections		
Frozen sections done	111	(62.4)
- in cases with positive margin (n=41)	22	(53.7)
- In cases with intermediate margin (n=19)	14	(73.7)
- In cases with negative margin (n=118)	75	(63.6)

¥ More than one surgical procedure possible

Table 2: Multivariate logistic regression analysis of surgical margin status in permanent sections of oral and lip squamous cell carcinoma

	Positive surgical margin (n=41)				Intermediate surgical margin (n=19)				Negative surgical margin (n=118)			
	No. of cases	**Odds Ratio**	**95% CI**	**p Value**	**No. of cases**	**Odds Ratio**	**95% CI**	**p Value**	**No of cases**	**Odds Ratio**	**95% CI**	**p Value**
Frozen sections done	22	0.70	0.31 – 1.61	0.40	14	1.26	0.39 – 4.07	0.70	75	1.15	0.56 – 2.37	0.70
pT-Stage												
pT1*	10	-	-	-	9	-	-	-	64	-	-	-
pT2	10	1.72	0.61 – 4.83	0,31	9	1.39	0.47 – 4.09	0.55	34	0.57	0.25 – 1.29	0.18
pT3	4	4.44	0.97 – 20.35	0.055	1	0.77	0.08 – 7.76	0.83	5	0.33	0.08 – 1.38	0.13
pT4	17	5.61	1.98 – 15.87	0.001	0	-	-	-	15	0.42	0.16 – 1-07	0.07
Grading												
G1*	5	-	-	-	2	-	-	-	21	-	-	-
G2	27	1.43	0.41 – 4.91	0.57	12	1.35	0.26 – 7.07	0.72	69	0.76	0.27 – 2.14	0.61
G3	9	1.03	0.25 – 4.23	0.97	5	1.21	0.19 – 7.68	0.84	28	1.02	0.32 – 3.32	0.97
Tumourlocalisation												
Lower jaw*	19	-	-	-	5	-	-	-	23	-	-	-
Floor of mouth	7	0.49	0.16 – 1.47	0.20	7	1.44	0.37 – 5.57	0.59	20	1.35	0.53 – 3.47	0.53
Tongue	3	0.21	0.05 – 0.84	0.03	3	0.39	0.08 – 1.83	0.23	33	4.70	1.55 – 14.23	0,01
Upper/lower lips	2	0.42	0.08 – 2.30	0.32	1	0.38	0.04 – 3.70	0.40	12	3.07	0.72 – 13.11	0.14
Upper jaw new	8	0.77	0.25 – 2.35	0.64	1	0.20	0.02 – 1.88	0.16	20	2.09	0.75 – 5.85	0.16
Other locations	2	0.57	0.10 – 3.14	0.52	2	0.73	0.12 – 4.52	0.73	10	1.80	0.46 – 7.06	0.40

* Baseline

Table 3: Multivariate logistic regression analysis about circumstances when frozen sections were taken

	Frozensections done (n=111)			
	No of cases	Odds ratio	95% CI	p Value
pT-Stage				
pT1*	48	-	-	-
pT2	40	2.53	1.12 – 5.74	0.03
pT3	8	4.03	0.76 – 21.25	0.10
pT4	15	0.78	0.31 – 1.95	0.59
Grading				
G1*	16	-	-	-
G2	64	0.77	0.31 – 1.94	0.58
G3	31	1.66	0.55 – 5.01	0.36
Tumour localisation				
Mandible*	25	-	-	-
Floor of mouth	25	2.15	0.79 – 5.88	0.14
Tongue	24	1.32	0.51 – 3.45	0.57
Upper and lower lips	11	2.62	0.68 – 10.14	0.16
Upper jaw new	15	0.82	0.30 – 2.22	0.69
Other locations	11	3.19	0.71 – 14.33	0.13

* Baseline

Table 4: Characteristics of frozen sections in patients with positive or intermediate surgical margins in permanent slides

	Positive surgical margin (n=41)		Intermediate surgical margin (n=19)	
	No of cases	**(%)**	**No of cases**	**(%)**
Frozen sections done	22	(53.7)	14	(73.7)
- positive (initial)	8	(36.4) *	1	(7.1)
- intermediate (initial)	3	(13.6) *	6	(42.9)
- negative (initial/after further frozen sections)	14	(63.6)	8	(57.1)
- same area as positive surgical margin	5	(22.7)	11	(78.6)
- other area as positive surgical margin	17	(77.3)	3	(21.4)

* one case showed dysplasia and carcinoma in frozen sections

Table 5: Univariate logistic regression analysis about different surgical-procedures and the surgical margin status.

	Positive surgical margin (n=41)				Intermediate surgical margin (n=19)				Negative surgical margin (n=118)			
	No. of cases	**Odds Ratio**	**95% CI**	**p Value**	**No. of cases**	**Odds Ratio**	**95% CI**	**p Value**	**No. of cases**	**Odds Ratio**	**95% CI**	**p Value**
Operations												
Local resection*	16	-	-	-	14	-	-	-	38	-	-	-
Hemimaxillectomy/ Upper jaw alveolar resection	6	0.93	0.33 – 2.74	0.93	1	0.17	0.02 – 1.33	0.09	20	2.03	0.77 – 5.37	0.15
Floor of mouth/ Tongue resection	4	0.42	0.13 – 1.32	0.14	1	0.14	0.02 – 1.08	0.06	29	4.19	1.48 – 11.83	0.01
Lower jaw resection	16	1.92	0.87 – 4.25	0.11	4	0.44	0.14 – 1.46	0.18	27	0.83	0.40 – 1.72	0.61
Other operations	1	0.45	0.05 – 3.84	0.46	0	-	-	-	7	5.06	0.60 – 42.91	0.14

* Baseline

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