

RESULTS OF RADIATION THERAPY IN ORAL SQUAMOUS CELL CARCINOMA

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Oral carcinoma constitutes 0.5 to 1.0 per cent of malignant tumours (SEGI 1977). Its incidence in most European countries, and in some other countries as for example Japan and New Zealand, is estimated to be between 2 and 4 new cases in males and approximately 2 new cases in females per 100 000 inhabitants and year (HIGGINSON & MUIR 1973, SEGI). The highest incidence rates are reported in India (SEGI). The incidence rates of oral carcinoma in Poland in 1976 were 1.6 new cases in males and 0.5 new cases in females per 100 000 and year (PAWLEGA & URBĄSKA 1979).

Surgery, and interstitial and external radiation therapy, as a single method or in combination, are the main treatment modalities in early and moderately advanced cases (HIRATA et coll. 1975, BAILLET & SOUDANT 1976, JESSE & FLETCHER 1977, POINTON 1977, SEYDEL 1977, LINDBERG & FLETCHER 1978). The 5-year survival rates in early cases as reported from the major oncologic centers, amount to 70 to 80 per cent (BAILLET & SOUDANT, LINDBERG & FLETCHER).

The main treatment method for patients with advanced inoperable oral carcinoma is external radiation therapy. However, the cure rate is low, with reported 5-year survival rates between 0 and 15 per cent (GILBERT et coll. 1975, HIRATA et coll., FU et coll. 1976, LANGDON et coll. 1977, POINTON, FAZEKAS et coll. 1980).

An analysis of results and causes of failure of radiation therapy in patients with oral carcinoma treated at this institute is now presented.

Material and Methods

From April 1967 to March 1976, 153 patients (127 men, 26 women; mean age 56.5 years, range 31 to 75) with previously untreated, microscopically confirmed squamous cell carcinoma of the oral cavity were irradiated with radical intention. The mean duration of symptoms was 5 months with a range from 1 to 24 months.

The site of the primary tumour and the stage distribution (UICC 1975) are presented in Table 1. The oral tongue was the most frequent site (51%), followed by the floor of the mouth and the buccal mucosa, while carcinoma of the lower gingiva and hard palate was infrequent (5.9%).

Stages III and IV constituted 68.8 per cent of the analysed group. The highest proportion of advanced cases was observed in patients with carcinoma in the floor of the mouth and in the tongue. All malignancies in the lower gingiva (6 patients) were advanced.

The status of the primary tumour and regional lymph nodes is presented in Table 2. Ten patients had stage I disease (6.5%), 38 stage II (24.8%), 61 stage III (39.9%) and 44 stage IV (28.8%). Clinically metastatic neck nodes were found in 76 patients (49.7%) at the beginning of treatment. The analysed group of radically treated patients contained no patients with distant metastases.

The methods of treatment in relation to clinical

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stage appear in Table 3. Twenty-nine patients with early oral carcinoma, stage I and II, received interstitial treatment with ²²⁶Ra needles. The tumour dose was 60 to 80 Gy in 120 to 180 hours. Interstitial treatment was also given in 2 patients with advanced malignancy, stage IV, in combination with neck dissection of the involved nodes.

Three patients with early carcinoma of the buccal mucosa received orthovoltage roentgen irradiation. One single portal was irradiated, and the given dose was 60 to 70 Gy in 5 to 6 weeks. All the other patients (119; 77.8%) received ⁶⁰Co teletherapy. Of these, 87 were treated with conventional fractionation (5 fractions/week). The tumour dose in most cases was 60 Gy in 5 to 6 weeks. In 32 patients with very advanced malignancy a combination of methotrexate and split-course irradiation was used. They received 25 mg methotrexate intravenously twice a week up to a total dose of 100 to 150 mg, and ⁶⁰Co irradiation up to a tumour dose of 40 Gy in 16 to 20 fractions over 3 to 4 weeks, followed by an interval of 3 to 4 weeks, and a new series of ⁶⁰Co treatment with 30 to 40 Gy in 12 to 16 fractions during 2 to 4 weeks. Further details concerning the techniques of irradiation have been published previously (SKOŁYSZEWSKI et coll. 1975, 1976).

Complications. Necrosis of the mandible developed 12 and 16 months after treatment in 2 of 32 patients treated with interstitial radium implantation. One patient in this group developed necrosis in the irradiated part of the tongue. The necrosis healed in all cases, after conservative treatment, and the patients survived for more than 5 years without evidence of malignancy.

In 4 patients (4.6%) in the group of 87 patients treated by conventional fractionation, necrosis of the mandible was observed; on an average 18 months after the end of treatment. Three of these patients were operated upon, and one patient was treated conservatively. All survived more than 5 years without evidence of carcinoma.

In the 32 patients with advanced malignancy, treated by the combined method (methotrexate plus split-course irradiation), complications occurred in 6 cases (18.8%). Two patients had a severe mucosal reaction after a full dose of methotrexate, 2 developed severe thrombocytopenia with bleeding during the methotrexate therapy, and 2 patients had bleeding from the ulcerated tumour necessitating ligation of the external carotid artery.

No deaths due to complications occurred.

Table 1

Site of the primary tumour and clinical stage in 153 patients

Site	Stage				Total	
	Early (I+II)		Advanced (III+IV)		No.	Per cent
	No.	Per cent	No.	Per cent		
Buccal mucosa	9	5.9	17	11.1	26	17.0
Lower gingiva	—	—	6	3.9	6	3.9
Hard palate	2	1.3	1	0.7	3	2.0
Oral tongue	31	20.3	47	30.7	78	51.0
Floor of mouth	6	3.9	34	22.2	40	26.1
Total	48	31.4	105	68.6	153	100.0

Table 2

Status of the primary tumour and regional lymph nodes. Roman letters indicate clinical stage

Primary tumour	Regional lymph nodes				Total
	N0, N1a, N2a	N1b	N2b	N3	
T1	10 (I)	—	—	—	10
T2	38 (II)	6 (III)	3 (IV)	4 (IV)	51
T3	29 (III)	26 (III)	18 (IV)	19 (IV)	92
Total	77	32	21	23	153

Results

The 5-year crude survival rate without evidence of malignancy was used for the evaluation. The results according to clinical stage, site and local extension of the primary tumour, and state of the regional lymph nodes appear in Table 4.

Forty-two patients (27.5%) survived for 5 years without evidence of disease. A statistically significant correlation existed between survival and clinical stage of the disease, local extension of the primary tumour, and clinical stage of the regional lymph nodes. No statistically significant differences existed between the results obtained in patients with different sites of the primary tumour.

The results according to the method of irradiation appear in Table 5; the data confirm the correlation between the results and the clinical stage. Of the

Table 3*Methods of treatment in relation to clinical stage of the disease*

Method	Stage				Total	
	Early (I+II)		Advanced (III+IV)		No.	Per cent
	No.	Per cent	No.	Per cent		
Interstitial treatment	29	18.9	2	1.3	31	20.2
Orthovoltage roentgen	1	0.7	2	1.3	3	2.0
⁶⁰ Co teletherapy, conventional fractionation	18	11.8	69	45.1	87	56.9
Methotrexate and split-course therapy	—	—	32	20.9	32	20.9
Total	48	31.4	105	68.6	153	100.0

Table 4*Five-year symptom free survival, stage of disease, site and extension of primary tumour and status of regional lymph nodes*

Clinical features	No. of cases	5-year survival without evidence of malignancy	
		No.	Per cent
Stage of disease			
UICC 1975			
I	10	9	90.0
II	38	19	50.0
III	61	13	21.3
IV	44	1	2.3
Site of primary tumour			
Buccal mucosa	26	8	30.8
Lower gingiva	6	0	0
Hard palate	3	1	33.3
Oral tongue	78	23	29.5
Floor of mouth	40	10	25.0
Local extension of primary tumour			
T1	10	9	90.0
T2	51	24	47.1
T3	92	9	9.8
Status of regional lymph nodes			
N0, N1a, N2a	77	33	42.9
N1b	32	8	25.0
N2b	21	1	4.8
N3	23	0	0
Total	153	42	27.5

patients treated with interstitial radium implantation 64.5 per cent survived for 5 years without evidence of disease. In this group 93.5 per cent of the patients had early carcinoma in clinical stages I and II.

Nineteen (21.8%) of those treated with a continuous course of external irradiation survived for 5 years without evidence of disease, and most of them had advanced carcinoma in stages III and IV. The results obtained in the patients treated with methotrexate combined with split-course irradiation were poor; only 9.4 per cent of them survived for 5 years without evidence of malignancy. It should be emphasized, however, that in this last group the disease was very advanced. Most patients with such advanced carcinoma previously received only palliative treatment.

The treatment failures are given in Table 6. The 111 patients analysed comprised 105 patients who died of carcinoma, 3 who died of cardiac failure without evidence of malignancy, and 3 in whom the cause of death remained unknown. Ninety-six patients (86.5%) died because of local recurrence of the primary tumour or regional lymph node metastases. In 9 patients, distant metastases were observed.

Management of clinically non-metastatic neck nodes. In the 153 patients analysed, the neck nodes were clinically negative on admission in 77 patients (50.3%). During a 5-year observation period development of metastases in the neck nodes was observed in 15 of 31 patients (48.4%) who did not receive elective irradiation of the neck and in 5 of 44 patients (11.4%) who received such treatment. The difference between these two groups was highly

Table 5
Five-year symptom free survival in relation to method of radiation therapy

Method	Early carcinoma (I+II)			Advanced carcinoma (III+IV)			Total		
	No. of cases	5-year survival		No. of cases	5-year survival		No. of cases	5-year survival	
		No.	Per cent		No.	Per cent		No.	Per cent
Interstitial treatment	29	19	65.5	2	1	50.0	31	20	64.5
Orthovoltage roentgen	1	0	0	2	0	0	3	0	0
⁶⁰ Co teletherapy, conventional fractionation	18	9	50.0	69	10	14.5	87	19	21.8
Methotrexate + split-course therapy	0	—	—	32	3	9.4	32	3	9.4
Total	48	28	58.3	105	14	13.3	153	42	27.5

significant ($p<0.001$). The two groups compared were not randomized. It should be emphasized, however, that the patients who received elective irradiation had in general locally more advanced malignancy than those in the other group and consequently should have had a high risk of developing neck node metastases. Five patients in the electively treated group developed metastatic neck nodes. In 3 of these cases the metastases developed behind the irradiated neck field, and in 2 cases the radiation dose was lower than 50 Gy.

Discussion

The survival rates observed in this series are in good agreement with results reported by several other authors (GILBERT et coll., HIRATA et coll., FU et coll., LEES 1976, LANGDON et coll., LINDBERG & FLETCHER, VOLTERRANI et coll. 1978).

The majority of the patients in the present series received ⁶⁰Co teletherapy. The results of telecobalt therapy (combined with methotrexate) in patients with loco-regionally advanced carcinoma were, however, very poor. The main cause of failure in these cases was local recurrence within the irradiated volume. There could thus exist possibilities to improve the results by improvement of the therapeutic ratio, for example by the use of high LET particle therapy, combination of radiation therapy with intensive multidrug chemotherapy, optimization of the fractionation schedules, and the use of radiation sensitizing substances.

The approach to the management of clinically

Table 6
Causes of treatment failure in 111 patients

Cause of treatment failure	No. of cases	Per cent
Local failure		
Local recurrence	51	46.0
Local recurrence and regional lymph node metastases	35	31.5
Regional lymph node metastases	10	9.0
Distant metastases		
Distant metastases only	6	5.4
Distant metastases and local recurrence and regional lymph node metastases	3	2.7
Other causes (cardiac failure)	3	2.7
Unknown	3	2.7
Total	111	100.0

non-metastatic neck nodes was in the present series related to the method of therapy of the primary lesion. In patients given interstitial treatment non-metastatic nodes were as a rule not irradiated. In patients treated with external telecobalt therapy the superior and sometimes the middle group of the neck nodes were usually included in the irradiated volume.

Patients who received irradiation of clinically non-metastatic neck nodes had a much lower incidence of clinical neck node metastases during the observation time than those who did not receive such irradiation. Even patients with early oral carci-

noma had a marked risk of developing neck node metastases if this region was not initially irradiated. A dose of 50 Gy in 5 weeks seemed to be high enough to eradicate subclinical disease and to prevent further manifestation of regional metastases. This observation is in agreement with some other reports (GILBERT et coll., BAILLET & SOUDANT, FU et coll., JESSE & FLETCHER).

SUMMARY

Between 1967 and 1976, 153 patients with previously untreated squamous cell carcinoma of the oral cavity received radiation therapy, either interstitial irradiation or external beam therapy (usually ^{60}Co). Five-year survival rates without evidence of disease were 90 per cent in stage I, 50 per cent in stage II, 21.3 per cent in stage III, and 2.3 per cent in stage IV. Thirty-one patients with clinically non-metastatic neck nodes not prophylactically irradiated had a high incidence of later metastatic neck disease compared with patients who received elective irradiation of the neck.

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