



Management of Early Oral Cavity Cancer. Experience of Centre Oscar Lambret

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From 1974 to 1983, 579 patients presenting with early oral cancer (excluding lip tumours) were treated at Centre Oscar Lambret. Of these, 429 were treated locally by brachytherapy with local control achieved in 82% of the cases (90% after salvage surgery). Treatment-related complications occurred in 19% of the cases, requiring surgical management in 13 patients. In contrast, only 51% of the 35 patients treated by external radiotherapy and brachytherapy were controlled, resulting in a poor 5-year survival (14%). Results for the 24 patients treated surgically were similar to those of brachytherapy alone. Finally, for T1 T2 N0 patients, the advantages of an elective neck dissection are not clear and could be clarified by a randomised trial. Indeed, this retrospective study failed to find a significant difference in the incidence of death due to an uncontrolled neck evolution whatever the neck management.

Keywords: oral cancer, early stages, brachytherapy, surgery, neck dissection, metachronous cancers.

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INTRODUCTION

ORAL CANCERS are frequent in northern France: the average annual incidence is 16.2 per 100 000 inhabitants (15.0 per 100 000 males and 1.2 per 100 000 females). At Centre Oscar Lambret, the Northern France Comprehensive Cancer Center, we are concerned with the management of oral cancer since it represents about one third of our activity in head and neck cancer. As a general rule, oral cancers are usually diagnosed at an early stage since the presenting symptoms are suggestive and the oral cavity is easily clinically examined. Surgery or local radiotherapy are the most common therapies for early tumours. The need for the best local control with the best possible functional results is the basis of decision making with, as a background, the risk of metachronous cancers which will also require active treatments. We retrospectively analysed our experience in early oral cancer management in a series of 579 patients treated over a 10-year period (January 1974–December 1983).

MATERIALS AND METHODS

Population

From 1974 to 1983, 5445 new squamous cell carcinomas (SCC) of the head and neck were referred to Centre Oscar

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Table 1. Oral cancer distribution (Centre Oscar Lambret, 1974–1983)

	Overall population	Selected*
Oral tongue	744	598
Floor of mouth	681	446
Lower gum	204	147
Upper gum and hard palate	71	41
Total	1600	1242

*Patients without previous or simultaneous cancer.

Lambret. Of them, 1600 were localised in the oral cavity. The most frequent primary sites (Table 1) were the oral tongue (OT) (anterior two thirds of the tongue or mobile tongue) and the floor of the mouth, both together representing 82.5% of the cases, more than the lower gum (13%) and, even more, than the upper gum and hard palate (4.5%). Considering only the selected population (in other words, patients who had no previous history of malignancy and no simultaneous cancer), 1232 patients remained in the analysis with a similar distribution of primary sites.

Early diseases were defined as T1 or T2 lesions with N0 necks (UICC recommendations for clinical staging, 1987) or with palpable lymph node(s) judged resectable by the surgical team. In addition, only for the OT and the floor of the mouth (FM), were very superficial T3 included in this analysis. 593 patients met these criteria. This population consisted of 350 early OT SCC (58.5% of all stages of OT tumours in the selected population), 208 early SCC of FM (47% of all stages),

21 early lower gum (LG) SCC (14% of all stages) and 14 early SCC of the upper gum or the hard palate (34% of all stages). This study focused only on SCC of the lower part of the oral cavity (LG, FM and OT), that is to say on 579 patients. There were 522 (90%) males and 57 (10%) females with a mean age of 54.5 years (range 29–87) at the time of diagnosis.

At Centre Oscar Lambret, during that period of time, early oral cancers were treated by surgery each time the tumour reached the bone, even superficially. All other cases were eligible for brachytherapy (BT) rarely preceded by an external radiotherapy (XRT) course. Only a few cases not suitable for BT due to the bone proximity but ineligible for surgery (due to general contraindications for such a surgery performed under general anaesthesia) were treated by external XRT. In other words, all T1T2 tumours of the LG were candidates for surgery in the absence of contraindication. All T1T2 tumours of the OT or of the FM remaining at a minimum of half a centimetre from the mandible were eligible for BT or, when the mandible was reached, for surgery. In addition, some selected cases of really superficial tumour slightly over 4 cm in diameter ("little" T3) were also treated by BT.

In all cases of OT, FM or LG diseases treated by surgery or BT, an elective or therapeutic management of the neck was associated. These neck dissections were performed at the time of primary resection or some weeks after the BT.

The initial evaluation consisted of a panendoscopy under general anaesthesia with, in most cases, a joint examination of the primary during this anaesthesia by both a radiation specialist and a head and neck surgeon. In addition, a thorough care of the dental status was performed before decision making.

Surgical procedures

Those rare limited tumours of the OT or FM remaining at some distance from the mandible which were operated on (the young age of the patient, or the need of a rapid and simple treatment due to elderly or social or geographical considerations, or the wishes of the patients having been taken into account for such a decision making) were resected by transoral electrosurgery, marginal glossectomy or pelviglossectomy. Tumours reaching or covering the mandible were treated by marginal mandibulectomy, extended to the FM or OT according to tumour extension and carcinological purposes. In the case of tumours of the alveolar ridge, at least two uninvolved tooth sockets were resected. Since there was no clinical bone invasion we never performed segmental mandibulectomy but some hemimandibulectomies were performed for tumours of the very posterior part of LG and, in particular, of the retromolar trigone. Each time it was possible 1–1.5 cm sound mucosal margins were ensured and were assessed by frozen sections. We did not perform any bone repair. When a direct closure of the mucosa was not possible we used a unilateral or bilateral nasolabial skin island flap(s) or, more recently, a platysma myocutaneous flap. Neither major pectoralis myocutaneous flap nor free transfers with microvascular anastomoses were used, in our institution, for these early stages.

Neck dissection consisted of a supra-omohyoid neck dissection (so-called triangular neck dissection) in the case of a T1N0 lesion or of a classical neck dissection in all other cases. This neck dissection was a functional procedure in the case of N0 neck or in the case of a lymph node below 2 cm in diameter.

Each time there were peroperatively several suspicious lymph nodes or when a lymph node was 2 cm or more in diameter, a radical procedure was performed. When the midline was reached by the tumour, a bilateral neck dissection was the standard practice.

Brachytherapy

Only Iridium-192 sources with an average energy of 0.3 MeV and the plastic loop method (described by Henschke in 1956) were used during this period of time. A meticulous step by step procedure is mandatory to ensure both good local control and limited side-effects. Implantation was performed under general anaesthesia. First, empty stainless steel needles were inserted in parallel positions and at appropriate distances from each other in order to obtain a regular distribution and to encompass the tumour and the requested surrounding volume (the target volume) to be carcinologically satisfactory. Thereafter, unloaded plastic tubes were placed through these needles and, then, needles were removed. The third step consisted of the setting up, through the plastic tubes, of "dummy" wires in order to check, under an intensifier screen, whether the implantation fitted or not the "Paris system" (i.e. parallel and equidistant lines in order to obtain a fairly regular dose distribution). If the implantation was satisfactory, the plastic loops were afterloaded with ¹⁹²Ir wires of similar radioactivity (again with the aim of homogeneity in irradiation) secured with metallic buttons. Afterwards, a dosimetry control on antero-posterior and lateral roentgenograms with computerised space reconstruction was performed and a dose of 60 to 70 Gy at the reference isodose for 4–8 day duration was given. Sources were removed without general anaesthesia.

External XRT

Definitive XRT was performed using photon beams of Cobalt 60 teletherapy machines or of linear accelerators of 5 to 10 MeV with two lateral opposite and parallel portals delivering 70–75 Gy to the primary with a classical fractionation (1 fraction of 2 Gy per day, 5 days per week). When a dose of 45 Gy had been reached, there was a field reduction in order to spare the spine. On the neck, a prophylactic dose of 50 Gy was delivered in the case of N0 neck, up to 70–75 Gy in the case of palpable lymph node(s).

When an external XRT prior to BT had been decided, this XRT was stopped when a dose of 45–50 Gy had been reached with a similar technique.

Postoperative XRT to the operative field was delivered only in the case of infiltrating T2 lesions of the FM or OT and in the case of positive or suspicious margins on the paraffin sections (whatever the primary site) and the radiation dose was of about 65 Gy. On the other hand, postoperative XRT to the neck was delivered only in the case of multiple N+ without extracapsular spread (55 Gy) or of at least one N+ with capsular rupture (55 Gy on the overall neck, up to 65 Gy on R+ areas).

Follow-up policy

Patients were clinically evaluated every week during XRT and after BT (in that case the mucosal reaction disappearance and healing was the best criteria for performing the subsequent neck dissection, as a general rule 4–6 weeks after implantation).

After the overall treatment, patients had a clinical evaluation

every 3 months and a chest X-ray (and, if possible, an oesophagofibrescopy) every 6 months until the 5th year of follow-up. Thereafter they were examined every 6 months with a yearly chest X-ray.

Statistical considerations

Clinical staging was made according to the UICC 1987 classification. Survival rates were calculated according to the Kaplan-Meier method, and comparison of survival according to the log-rank test. The survival was evaluated from the day of pathological diagnosis. The comparison of effects was statistically checked with the χ^2 test.

RESULTS

Over this 10-year period, among these 579 selected patients with early primary, 92 patients (16%) had surgery on the primary, 429 patients (74%) were treated by BT alone, 35 patients (6%) by external XRT followed by BT while 23 patients (4%) received only, for general considerations, external XRT (Table 2).

Surgery

24 SCC of the OT, 47 of the FM and 21 of the LG were operated on. Surgery consisted of transoral electrosurgery in 12 patients (2 LG, 5 FM and 5 OT), of marginal glossectomy in 14 patients (14 OT), of pelviglossectomy in 15 patients (10 FM and 5 OT), of marginal mandibulectomy in 4 patients (4 LG) with pelviglossectomy in 32 patients (32 FM) while we performed a hemimandibulectomy (so-called "commando") in 12 LG patients. There were 25 T1 and 67 T2, 66 patients were classified N0 and 26 had palpable lymph nodes.

There were no treatment-related deaths. On paraffin sections margins were free in all but 2 cases (2%). Local recurrences occurred in 18 patients (19.5%) of the cases (Table 3). Of these recurrences, 8 could be controlled by a subsequent "re-surgery". The final control was of 82/92 (89%). Control of the neck was achieved in 79/92 patients (86%) at the first attempt and, after successful salvage in 81/92 patients (88%). Distant metastases occurred in 5 patients and second primaries in 20 patients (22%).

The 3-year absolute survival was 64%, the 5-year was 42% and the 10-year was 26%. The causes of death were an evolution of the oral cancer in 18 patients; a metachronous cancer in 23 patients; an intercurrent disease in 9 patients; and an unknown cause in 15 patients.

Brachytherapy

429 patients were treated by ^{192}Ir . BT (283 SCC of OT and 146 of FM). There were 143 T1 (31%), 246 T2 (57%) and

Table 2. Early oral cancer management (Centre Oscar Lambret, 1974-1983)

	Surgery	BT	XRT + BT	XRT
Oral tongue	24	283	29	14
Floor of mouth	47	146	6	9
Lower gum	21	—	—	—
Total	92	429	35	23

BT = Brachytherapy; XRT = external radiotherapy.

Table 3. Surgery for early oral cancer (Centre Oscar Lambret, 1974-1983)

	LG	FM	OT	Total
Local failure	2/21 9.5%	11/47 23%	5/24 21%	18/92 19.5%
T1	0/3	2/9	0/3	2/15 13%
T2	2/18	9/38	5/21	16/77 21%
Successful salvage surgery	1/2	4/11	3/5	8/18
Final local control	20/21 95%	40/47 85%	22/24 92%	82/92 89%

LG = Lower gum; FM = floor of mouth; OT = oral tongue.

Table 4. Local failures after brachytherapy alone (Centre Oscar Lambret, 1974-1983)

	FM	P value	OT	Total	
T1	5/53 9.5%	NS	11/81 13.5%	16/134 12%	} NS } P = 0.002
T2	16/76 21%	NS	27/170 16%	43/246 17.5%	
T3	8/17 47%	NS	10/32 31%	18/49 38%	
Total	29/146 20%	NS	48/283 17%	77/429 18%	

*FM = Floor of mouth; †OT = Oral tongue.

49 T3 (12%), while 354 (82.5%) did not have palpable lymph node. 49 (11.5%) were classified as N1, 22 (5%) as N2 and finally 4 (1%) as N3. Patients underwent a mean dose of 64 Gy (ranging between 50 and 80 Gy). More precisely, T1 patients received a mean dose of 61 Gy, T2 of 64 Gy and T3 of 69 Gy. In addition, 227 patients had a unilateral neck dissection (ND), 152 a bilateral ND, 5 a prophylactic XRT on the neck and 45 (10.5%) did not have surgery on the neck nor XRT but were simply observed at this level, at least as a first approach.

Two months after completion of the overall treatment, 415 patients were alive and free of disease (97%), 8 (2%) had persistent local and/or regional disease and 6 (1%) had died.

Taking into account both persistent diseases and local recurrences (Table 4), the local control was achieved with BT alone in 352 patients (82%). There was no statistical difference between local control for T1 lesions (118 patients or 88%) and for T2 (203 patients or 82.5%). In contrast, local control for T3 was only 63% (31 patients) and the difference was highly significant ($P = 0.002$). Local recurrences occurred at a mean time of 23 months, ranging between 6 and 72 months.

These local failures were treated, whenever possible, by surgery. After successful salvage surgery, the final local control rates were 90% (390 patients) for the overall population, 96% for T1 (129 patients), 91% for T2 (225 patients) without significant statistical difference between T1 and T2 and 73% for T3 (36 patients) and statistically significant ($P = 0.0003$). In other words, surgery was able to cure 11/16

Table 5. Local control after brachytherapy (Centre Oscar Lambret, 1974–1983)

	After BT* alone		After BT + salvage surgery	
T1	118/134 88%	} NS	129/134 96%	} NS
T2	203/246 82.5%		225/246 91.5%	
T3	31/49 63%	} P=0.002	36/49 73.5%	} P=0.0003
FM†	117/146 80%		133/146 91%	
OT‡	235/283 83%	} NS	257/283 91%	} NS
Total	352/429 82%		390/429 91%	

*BT = brachytherapy; †FM = floor of mouth; ‡OT = oral tongue.

(69%) local recurrences for T1 lesions, 22/43 (51%) for T2 but only 5/18 (28%) for T3 for a total of 38/77 (49%). The final local control was achieved in 257/283 (91%) and 133/146 (91%) FM patients (Table 5). The control of the neck was achieved at first approach in 350 patients (82%) and after salvage treatment in 381 patients (89%).

Distant metastases occurred in 15 patients (3.5%) while 130 patients (30%) demonstrated metachronous cancers. To date, 160 additional SCC have been diagnosed: 110 were located on the upper aero-digestive tract, 26 in the lung, 18 on the oesophagus and 6 in various sites.

Brachytherapy-related complications occurred in 82 patients (19% of the overall population). The most frequent was a mucosal necrosis (47 patients = 11%), followed by osteoradionecrosis (21 patients or 5%), both (10 patients or 2%) and skin necrosis (4 patients or 1.5%). A simple medical treatment could overcome these local complications in 69 patients (84% of patients with complications). In the other cases, a transoral resection of a persistent ulceration on the implantation field was needed in 2 patients, while an osteoradionecrosis requested a marginal mandibulectomy in 6 patients or a hemimandibulectomy in 4 patients, in 1 case of skin necrosis a cutaneous flap was necessary. In total, surgical management for local side-effects was mandatory in 13 patients (3% of the population).

The 5-year absolute survival rate was 222/429 patients (52%), or more precisely, 82/34 (61%) for T1, 123/246 (50%) for T2 and 17/49 (34%) for T3 (T1 vs. T2 $P=0.03$, T1 or T2 vs. T3 $P=0.05$). Regarding the primary site, survivals did not vary: 78/146 (53%) for FM and 144/283 (51%) for OT.

The causes of death were tumour evolution in 89 patients (21%), 22 among them having died of local evolution, a second primary in 75 patients (17%), intercurrent disease in 69 patients (16%) or an unknown cause in 34 patients (8%). In addition, there were 6 treatment-related deaths (4 after BT and 2 after the neck dissection).

External XRT followed by BT

35 patients (6 FM and 29 OF) were treated by external XRT (45–50 Gy) followed by an ^{192}Ir implantation of the residual

Table 6. Local control after radiotherapy and brachytherapy (Centre Oscar Lambret, 1974–1983)

	Local failures	Successful salvage surgery	Final local control
T2	14/29	3/14	17/29
T3	3/6	1/3	4/6
FM*	3/6	1/3	4/6
OT†	14/29	3/4	17/29
Total	17/35 49%	4/17 23.5%	21/31 60%

*FM = floor of mouth; †OT = oral tongue.

disease (25–40 Gy) for a total dose to the primary of 75.2 Gy (ranging between 70 and 90 Gy). All of FM diseases were classified T2 while there were 23 T2 and 6 T3 OT diseases. In addition, palpable lymph nodes were found in 13 patients. There were no treatment-related deaths, local complications occurred in 5 cases (1 FM and 4 OT): all were cured by a simple medical treatment.

Local control after this combined modality was of 18/35 (51%). It was similar for OT and FM and for T2 and T3, more precisely in 3/6 FM vs. 15/29 OT and in 15/29 T2 vs. 3/6 T3. After successful salvage surgery the local control increased up to 21/35 (60%), in 4/6 FM and 17/29 OT, or in 17/29 T2 and 4/6 T3 (Table 6). This means that salvage surgery could only control 4/17 (23.5%) local failures. 4 patients demonstrated distant metastases and 7 patients a metachronous cancer.

At 3 years, the absolute survival was 13/35 (37%) and at 5 years 5/35 (14%). No patient survived for 10 years.

The causes of deaths were cancer evolution in 17 patients (14 due to an uncontrolled local evolution), a metachronous cancer evolution in 5 patients, an intercurrent disease in 6 patients while 2 patients died of unknown cause.

Definitive XRT

9 SCC of FM (4 T1 and 5 T2, 7 N0) and 14 of OT (1 T1 and 13 T2, 4 N0) were treated by external XRT with a mean dose of 63 Gy (55 to 75 Gy). After XRT for FM tumours, there were 2 relapses, 1 was controlled by a salvage surgery, the final local control was 8/9. In contrast, for OT the local control was poor: 4/14 and after salvage 5/14. During the follow-up, there were three second primaries but no patient demonstrated distant metastases.

4 patients were still alive at 3 years, none at 5 years. The causes of death were an evolution of the oral cancer in 13 patients, metachronous cancer in 3 patients, intercurrent disease in 7 patients and an unknown cause in 1 patient.

DISCUSSION

Our results are consistent with the current literature [1–6] and we did not have in mind, when we initiated this retrospective study, to compare different therapeutic options since selection of patients varies widely in published series. Therefore, our discussion will focus only on our thoughts about early oral cancer management at the close of this 10-year experience.

For the lower gum, surgery appears to be reliable. For OT SCC and FM SCC (remaining at distance from mandible), we have to take into account the local control rate, the incidence of

local complications, the reliability of salvage surgery and the final result. Brachytherapy is, for us, the most appropriate treatment, able to cure, by itself, 82% of early oral SCC. Attention should be paid, nevertheless, to some points. Though T1 and T2 were similarly controlled by BT alone (around 85% of the cases), in contrast, less than two thirds of "little" T3 were controlled (63%, $P=0.0003$). In addition, local complications were more frequent in T3 diseases (33 vs. 17% for T1T2, $P=0.01$). On the other hand, the combined modality XRT-BT achieved poorer results (local failures: 17/35 or 48.5% vs. 77/429 or 18%, $P=0.00001$) in particular for T2 (local control=52% vs. 82.5% after BT alone). Finally, salvage surgery was less successful for T3 relapses 6/21 or 28.5% than for T1T2 (31/73 or 42%) or for XRT-BT failures (4/17 or 23.5%) when compared to BT failures (38/77 or 49%; $P=0.05$). This explains that, nowadays, we have abandoned XRT-BT in all cases and BT for T3 lesions which are, in most cases, surgically treated. Surgery (and this conclusion is generally found in literature) achieved results comparable to those of BT. If functional results for limited resections were really acceptable and identical to BT, in contrast they were less satisfactory for more extensive procedures. As a result, surgery is proposed at Centre Oscar Lambret only for superficial tumours below 1 cm in diameter (in particular for young patients). Definitive XRT was used in specific cases and the selection of patients was unfavourable. Although in this selection, XRT could often control the primary when located on FM but rarely for OT tumours.

Finally, the elective treatment of the neck, in the case of early N0 disease, remains controversial in the absence of a large randomised trial. When operated on, N0 necks have been revealed to be histologically involved in about one third of the cases. On the other hand, excluding patients treated by XRT alone, 157 of the 556 other patients (28%, going up to 42% for T1N0 patients) demonstrated second primaries for a total of 194 additional cancers. Among these metachronous cancers, 134 (69%) were located on the upper aerodigestive tract. Clearly, it is mandatory to keep in mind the probable need for an alternative treatment above clavicles for another cancer, in other words, to keep open all options. This helps avoid unnecessary procedures for the treatment of the first malignancy if the disease is diagnosed early and free of clinical nodal metastasis. In this material we selected T2T2N0 patients who were treated by BT alone [indeed, in that case, the necks had not received any treatment before the neck dissection (ND) or the neck follow-up]. 278 patients underwent an elective ND. In 198 cases there was no histological nodal involvement. The clinical false negative rate was 29%, ranging between 35% for OT, 25% for FM and 5% for LG. During the same period, 64 patients had only a neck follow-up. Comparison of both groups (Table 7) failed to find statistical difference in final neck control. Among patients who had ND, 40 developed a neck recurrence (11/99 T1 and 29/179 T2) and 28 died of an uncontrolled neck evolution (8 T1 and 20 T2). Of the 67 patients who had only a nodal follow-up, 11 demonstrated a nodal appearance (1/28 T1 and 10/36 T2) and 8 died of an uncontrolled neck evolution (all T2). We have to underscore that, whatever the neck management, half of the recurrences in the neck were with a local relapse and half of the deaths due to

Table 7. Outcome of T1T2N0 patients treated by brachytherapy (Centre Oscar Lambret, 1974-1983)

	Neck dissection	Neck follow-up	P
Neck evolution			
T1	11/99 (11%)	1/28 (3.5%)	NS
T2	29/179 (16%)	10/36 (28%)	NS
Total	40/278 (14%)	101/64 (17%)	NS
With local failure	21/40	4/11	
Death due to neck evolution			
T1	8/99 (7%)	0/28	NS
T2	20/179 (11%)	8/36 (19%)	NS
Total	28/278 (10%)	8/64 (12.5%)	NS
With local evolution	14/28	4/8	
Mean survival (months)	84	36	0.00001
Causes of deaths			
Oral cancer	33/278	13/64	NS
Metachronous cancer	49/278	13/64	NS
Intercurrent	34/278	21/64	0.00009
Unknown	18/278	10/64	0.01

an uncontrolled neck evolution were also associated with an uncontrolled local recurrence. The mean survival varied significantly (84 vs. 36 months) but this difference did not correlate with a difference in oral cancer failure related death rate. It seems logical, when the compliance of the patient for a thorough follow-up is real and when their neck is easily palpable, to discuss (maybe under the form of a randomised trial) a more economical treatment keeping in reserve the ND for the possible nodal appearance.

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