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SELECTION OF PATIENTS FOR RE-IRRADIATION WITH LOCAL IMPLANTS IN CARCINOMAS OF OROPHARYNX AND TONGUE

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Abstract

Between 1972 and 1984, 123 patients with recurrent or new primary carcinomas in previously irradiated areas of soft palate, tonsil, base of tongue or mobile tongue were re-irradiated with iridium-192 afterloading techniques. The average re-irradiation dose was 62 Gy (31–84 Gy) and the total dose 131 Gy (92–162 Gy); only 28 cases of mucosal necrosis were observed (23%). Two and 5 years actuarial local control rates were 67% and 59% and survival rates 48% and 24% respectively. Death was related to local tumor in 48 cases, metastases in 8 cases and intercurrent disease in 39 cases. We analysed the effect on survival and local control of age, initial tumor site and volume, previous surgery, time between first irradiation and re-irradiation, doses, dose rate, and techniques of brachytherapy. With this analysis as background, we recommend the use of salvage brachytherapy for patients with a) small tumors of soft palate, tonsil or mobile tongue without synchronic lymph node metastases, b) long time interval between first irradiation and re-irradiation, c) new primary tumors (rather than recurrence of first tumor), and d) no previous local surgery. A high re-irradiation dose given with low dose rate is recommended.

Key words: Therapeutic radiology; re-irradiation, ^{192}Ir implant, oral and oropharyngeal carcinoma.

Head and neck tumors have fairly poor prognosis. Even when immediate local control is obtained, relapse or development of a second primary tumor are common. After the initial radiation therapy, surgical rescue is not always possible and therefore re-irradiation should sometimes be considered. Retreatment of head and neck tumor up to a total dose above 100 Gy is a challenge to the traditional rules of radiotherapy. A few publications demonstrate the practicability of this therapy (1, 2, 4, 5, 7, 8, 10).

Toxicity is relatively moderate and local control can be obtained in more than half of the patients, but the long-term survival rate is still rather low. One should therefore choose patients for whom a real benefit of the treatment could be expected. In 123 patients treated in Centre Alexis Vautrin we have analyzed prognostic factors influencing local control and survival. With this analysis as background, we have tried to define suitable criteria for selecting patients most likely to respond to this type of retreatment.

Material and Methods

From 1972 to 1984, 123 patients with squamous cell cancer in the mobile tonque or oropharynx within previously irradiated areas were treated with afterloading ^{192}Ir implants; in 72 patients the tumor was regarded as a local recurrence, while in the remaining 51 patients it probably represented a new primary tumor. Our usual treatment technique was used (3, 6). We have studied the rates of local control, complications and survival in relation to some factors of possible prognostic importance. The patient population had the following principal characteristics:

- site of first irradiated tumor: oropharynx 56, pharyngolarynx 35, and oral cavity 32 patients,
- site of re-irradiated tumor: tonsil 43, base of tongue 32, mobile tongue 26, and soft palate 22 patients,
- age at irradiation: 42 to 76 years,
- size of re-irradiated tumor: T1 35, T2 49, T3 38 and T4 one patient; 71 tumors were smaller than 3 cm and 52 tumors larger than 3 cm in diameter,
- lymph node status at re-irradiation: N0 82, N1 32 and N3 9 patients,
- previous local surgery: none in 67 patients, lymph node dissection in 15 and lymph node plus primary tumor surgery for initial tumor in 41 patients,

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- time between first tumor treatment and re-irradiation: 3 months to 20 years, mean 4.5 years,
- first treatment dose: 36–140 Gy, average 69 Gy,
- re-irradiation dose: 31 to 80 Gy, average 62 Gy,
- technique of brachytherapy: guide gutter 25 and plastic tubes 98 patients,
- dose rate: less than 8 Gy/day in 23, 8–16 Gy/day in 76, more than 16 Gy/day in 23 patients,
- iridium wire activity: average 1.83 mrhm,
- number of iridium wires in mid tumor plane: 1 to 12 lines.

Twelve patients were treated with a palliative intent because of large local recurrence or fixed lymph node metastases. The remaining 111 patients were treated with a curative intent.

Simple factor analysis was made with a computed logical program PIGAS (9). The statistical significance of differences was analyzed by log rank test or χ^2 test.

Results

Actuarial survival rates at 2 and 5 years were 48% and 24% respectively. The following factors were positively correlated with the survival rates: curative intent of treatment ($p=0.0001$), local control ($p=0.0001$), size of re-irradiated tumor smaller than 3 cm ($p=0.015$), new primary tumor and not a local relapse ($p=0.016$). Also the site of the re-irradiation had prognostic importance. The relative risk of death (compared to the whole material) was thus 0.7 for tonsil, 0.9 for mobile tongue, 1.0 for soft palate and 1.8 for base of tongue.

Patients without previous local surgery had a higher survival rate ($p=0.02$) and the same was true for patients with more than 2 years' interval between first treatment and re-irradiation ($p=0.03$).

Actuarial survival rate without local recurrence were at 2 and 5 years 67 and 59% respectively; the local control was positively correlated with curative intent of treatment ($p=0.0001$), size of the re-irradiated tumor less than 3 cm ($p=0.0016$), new primary tumor and not relapse of first irradiated tumor ($p=0.017$) and re-irradiation dose above 60 Gy ($p=0.05$).

Also the site of the re-irradiated tumor had importance; the 2-year control rates were for oral cavity, pharyngolarynx and oropharynx 78, 69 and 48% respectively ($p=0.0013$).

The complication rate was relatively low. We only observed 28 cases of mucosal necrosis (23%). As necroses we only included cases without synchronic or metachronic local relapse. Lymph node surgery before irradiation was associated with a higher risk of complication ($p=0.02$); we noted with and without previous node dissection complications in 47 and 12% respectively. If the tumor was located in the soft palate, we noted necrosis in only 5% compared to 21% in tonsil, 28% in base of tongue and 34% in mobile tongue.

The patients with necrosis received a higher total dose (average 137 Gy versus average 127 Gy), but this difference was not statistically significant.

Discussion

Before a curative salvage radiation therapy is decided, it is important to select suitable patients and to choose adequate technical parameters.

According to the present data, site, dose and volume of the first irradiation do not seem to have a great prognostic importance. However, one of the authors (2) has previously reported an influence of the initially irradiated volume on the local control rate. To judge from the present analysis the role of previous surgery seems to be more important. Initial node dissection was associated with a higher risk of necrosis and previous tumor surgery seemed also to have a negative effect on the survival rate after re-irradiation. The vascular changes induced by loco-regional surgery might be an explanation for this, in our series, significant association.

A long delay between first and second radiation treatment has previously been reported to have a positive effect on survival (1, 2, 5, 7, 8, 10) and a similar correlation was found in the present study. One explanation for this is certainly the fact that a short time interval between the first and second tumor often indicates high biological aggressiveness. Another factor may be recovery of the irradiated tissues.

Our finding that new primary tumors had better prognosis than recurrences has not previously been expressly pointed out, but also in two earlier reported series (3, 5) we found higher survival and local control rates in new primaries. A recurrence is probably often an expression of an aggressive tumor and it is also possible that a recurrence is less radiosensitive due to clonogenic selection, caused by the first radiation treatment.

As previously reported (3, 5) we found that re-irradiated carcinomas in the base of the tongue had worse prognosis than tumors in tonsil, soft palate and oral cavity. However, this may just be a confirmation of the generally bad prognosis for carcinoma of the base of tongue.

It is quite obvious that tumors with too large a volume for adequate retreatment or with synchronic fixed lymph node metastases cannot be cured by salvage local brachytherapy. However, even when the treatment was given with curative intent, we found, as in previous series (2, 5), that the complication and local recurrence rates were higher when the re-irradiated tumor was large.

According to the literature and to our own experience a dose above 60 Gy is as a rule necessary in order to obtain local control (1–3, 5, 7) and long-term survival (3, 5, 7, 8). This high dose necessarily induces a fairly high complication rate (3, 5). Even after lower doses, necrotic syndrome are not rare but they are usually associated with tumor relapse and cannot be considered as real complications.

Comparisons between external radiotherapy and brachytherapy for salvage re-irradiation (3, 4, 8) generally show a benefit for brachytherapy. This is quite natural as brachytherapy—and especially local implants—makes it possible to deliver a higher local dose with less exposure of surrounding tissues.

The detailed technique of brachytherapy has not been demonstrated to have a prognostic importance and in the present study we failed to find any correlation between local control rate and the number of wire lines in the mid tumor plane. A more elaborate analysis of the complex volume which has to be treated in oropharyngeal cancers could be of great interest. In our practical experience, the plastic tube technique seems to be the best method for adaptation of the treatment volume to the shape of the tumor. We also recommend a low dose rate using a low activity wire, but we have not found any correlation between the dose rate and the rates of local control and complications.

With our present experience and after this analysis, we can recommend for salvage re-irradiation patients with small tumors in soft palate, tonsil or mobile tongue without synchronous lymph node metastases, especially if there is a long time interval between first irradiation and re-irradiation, a new primary tumor rather than recurrence of the first irradiated tumor, and if no previous local or nodal surgery has been performed.

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