Therapeutic Results for 100 Patients with Cancer of the Mobile Tongue Treated with Low Dose Rate Interstitial Irradiation

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Abstract. Aim: To evaluate the conservativeness of low dose rate interstitial irradiation (LII) for cancer of the mobile tongue. Patients and Methods: Between 1975 and 2002, 100 consecutive patients (71 men, 29 women) underwent LII as curative treatment. Stages were I/II/III/IV=16/63/16/4. Seventy-one cases were treated with LII alone and 29 cases treated combined with external irradiation. Median total dose of LII was 70 Gy/7 days. Results: Overall, 5- and 10-year local control and LII-treated patients’ survival rates were 93% and 91%, 64% and 57%, respectively. Delayed neck metastases were observed in 21% of initially N0 cases, 56% of which could be salvaged by operation. Early stage and well-differentiated tumors carried better prognoses. Conclusion: LII of cancers of the mobile tongue results in good local control and survival. With careful monitoring of patients to ensure early detection of delayed metastases, LII should allow organ conservation and yield favourable therapeutic results compared with those of surgery.

Interstitial irradiation is a method of radiation therapy that is performed by inserting a small sealed source directly into a tissue and then delivering radiation inside a lesion. Interstitial irradiation from the small source enables treatment to be limited to the lesion. This therapeutic approach achieves a high local cure rate while requiring only a short treatment time and is minimally invasive to the surrounding tissues, such as the salivary glands and mandible in the case of application to cancers of the tongue. Unlike surgical operations, interstitial irradiation has the great advantage of conserving the form and function of the organ harboring the primary lesion. In addition, for patients with metastasis to the neck lymph nodes who hope for conservation of function at the primary lesion site, combined therapy consisting of surgical dissection of neck lymph nodes and interstitial irradiation can be performed. Interstitial irradiation can be either low or high dose rate. In the low dose rate method, the small source is inserted directly into the tumour, while in the high dose rate method a device is inserted into the tumour, position is confirmed and the small source is then inserted by a remote afterloading technique. The small sources employed for therapy include iridium 192, used for both low and high dose irradiation, and caesium 137, gold particles and radium 226, used for low dose irradiation. The most common application of interstitial irradiation is for the treatment of cancers of the tongue. This paper reviews the results obtained in our institution from treatment of tongue malignancies using low dose rate interstitial irradiation (LII) as an organ-conserving method.

Patients and Methods

Patients. Between 1975 and June of 2002, a total of 100 patients (71 men, 29 women) underwent LII as curative treatment for mobile malignancies of the tongue in the Departments of Oral Surgery and Radiology at Tokyo Metropolitan Komagome Hospital. All malignancies were squamous cell carcinomas. Mean age at the time of diagnosis was 56 years (range 15-87 years). The degree of histological differentiation was high in the large majority of patients (n=84), moderate in 11 patients and poor in 5 patients.

Staging of the primary lesion was performed on the basis of visual observation and palpation, with consideration also given to CT and MRI findings. Neck lymph nodes were examined by palpation, ultrasonography, CT and MRI. Classification of the patients according to T factor gave 1:2:3:4=16:64:46:4, while the N factor was 0:1:2:3:4=75:11:14. Staging results showed stage I for 16 patients, stage II for 63 patients, stage III for 16 patients and stage IV for 4 patients.

The mean duration of follow-up for survivors was 129 months (range, 5-312 months).
Interstitial irradiation. A $^{226}$Ra needle was used as the small source.

Interstitial irradiation alone was used for 71 patients. The disease stage was stage I in 12 patients, stage II in 40 patients, stage III in 16 patients and stage IV in 3 patients. The median total radiation dose was 70 Gy (range, 60-94.5 Gy).

The remaining 29 patients underwent combined therapy using external irradiation in addition to interstitial irradiation. The disease stage was stage I in 2 patients, stage II in 10 patients, stage III in 6 patients and stage IV in 11 patients. The median total dose of interstitial irradiation was 60 Gy (range, 30-70 Gy). For external irradiation, the median total dose was 50 Gy (range, 20-60 Gy).

External irradiation. N1-N2 lymph node metastases were detected in 26 patients. Radical neck dissection was performed on 23 of these patients and external irradiation was administered prior to dissection in 8 patients.

External irradiation was performed with 4-MV X-rays and the median total dose of bilateral opposing portal irradiation was 50 Gy (range, 20-60 Gy).

**Results**

**Local control rate.** The local control rate of overall cases was 93% after 5 years and 91% after 10 years.

On the basis of T factor classification, 5-year control rates were 100% for T1, 97% for T2, 77% for T3 and 0% for T4. On the basis of treatment modality, 5-year control rates were 93.9% for the interstitial irradiation alone group and 91.6% for the interstitial and external irradiation groups (n.s.).

**Survival rate.** As of June of 2002, 42 of the 100 patients had died. Cause of death was tongue cancer in 23 patients, while 10 patients died of a second malignancy and 9 died of other diseases.

Overall, 5- and 10-year survival rates were 64% and 57%, respectively (Figure 1). Survival rates for tongue cancer were 69% at 5 years and 67% at 10 years (Figure 2).

On the basis of disease staging, 5-year survival rates were 85% for stage I, 69% for stage II, 66% for stage III and 27% for stage IV (I+II+III vs. IV, $p<0.05$; Figure 3). On the basis of treatment modality, 5-year survival rates were 74.2% for interstitial irradiation alone group and 41.4% for interstitial and external irradiation group ($p<0.01$). This was mainly because the latter contained more advanced cases.

Initial classification was N0 for 75 patients, since no neck metastases were detected, but 21 of these patients (28%) later developed neck metastases. Salvage by surgical operation was performed for 15 of those 21 patients.

The 5-year survival rates differed significantly between highly differentiated primary lesions (69%) and moderately and poorly differentiated lesions (38%; $p<0.005$; Figure 4).

Among 75 patients who were initially N0, 16 (21%) developed delayed neck metastases between 1 and 25 months following interstitial irradiation. All received operation and 9 (56%) were salvaged and their 5-year survival rate was 56%. The 5-year survival rate for those who did not develop delayed neck metastases was 74%. There was no statistically significant difference between the two groups.

**Late-stage adverse experiences after irradiation.** Mandibular necrosis (Grade II according to NCI-CTC) was diagnosed as a late stage adverse experience in 3 patients (stages I, II and III, n=1 each).

**Discussion**

A search of the literature was performed for the local control rate for tongue cancers. Spiro and Strong (1) took a surgical approach and performed partial resection of tongue cancers, reporting local control rates of 85.1% for
Stage I, 77.0% for Stage II and 50% for Stage III lesions. Kamata (2) treated tongue cancers with $^{226}$Ra needle interstitial irradiation and recorded local control rates of 97.6%, 95.1% and 76.2% for T1, T2 and T3 respectively, superior to the results of 87.5% for T1 and 84.2% for T2 when they performed surgery. Yoshida (3) et al. also performed $^{226}$Ra needle interstitial irradiation and reported a local control rate of 92.7%. This rate is by no means inferior to that of surgical treatment (4) and they also noted that the interstitial irradiation-treated patient group excluded subsets of patients who were thought to have a relatively good prognosis, i.e., patients with lesions of diameter ≤1 cm and patients with cancerous lesions in a portion of the leukoplakia. In consideration of these facts, they concluded that $^{226}$Ra needle interstitial irradiation resulted in a truly excellent local control rate. In the present study, local control rates for tongue cancer were 100%, 97% and 77% for T1, T2 and T3, respectively, while form and function were conserved. These results indicate the potential of interstitial irradiation to provide treatment outcomes comparable to those provided by surgical approaches.

Our results showed a significant difference in the survival rate for highly differentiated lesions compared with moderately and poorly differentiated lesions. Most deaths resulted from neck lymph node and distant metastases. Since irradiation therapy is a local treatment, improved treatment results in patients with moderately and poorly differentiated cancers of the tongue may require a multidisciplinary approach, such as concomitant administration of chemotherapy.

Delayed metastases were detected in 21% of N0 patients, and the 5-year survival rate in these patients was 56%. On the other hand, the 5-year survival rate for those who did not develop delayed neck metastases was 74%. There was no statistically significant difference between the two groups in this study. Conflicting results have been reported regarding the significance of preventive dissection of neck lymph nodes in N0 patients. Interstitial irradiation is a treatment that does not involve surgery (5-8). Thus, if preventive neck lymph node dissection had been performed for all of our patients, the approximately 80% remaining would have undergone unnecessary surgery, since delayed metastases did not develop. In this light, we surmise that careful analysis of patients with cancer of the tongue should be performed for risk factors associated with the development of delayed neck metastases. Moreover, a randomized controlled trial is necessary to evaluate the necessity of prophylactic neck dissection.

Interstitial irradiation of cancers of the tongue results in good local control and survival rates, while the adverse effects are tolerable (9-11). With careful monitoring of patients to ensure early detection of local recurrence and delayed metastases, interstitial irradiation should allow preservation of form and function and yield therapeutic results that compare favourably with those of surgery.

References


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