Abstract. 
Background: Surgical treatment remains the mainstay therapy for recurrence of head and neck cancer after previous radiotherapy. In inoperable cases, interstitial high-dose rate brachytherapy is a treatment option for local dose escalation. Patients and Methods: A retrospective analysis of all patients who were treated solely with brachytherapy for advanced non-resectable recurrences of squamous cell carcinomas of the head and neck and who previously received radiotherapy was performed. Results: A total of 12 patients with advanced recurrences were treated with interstitial brachytherapy with a fraction dose of 2-3 Gy and a total focal dose of 20-33 Gy. The shortest survival after brachytherapy was 4 weeks. The longest clinical course without evidence of local recurrence is 4 years and 11 months. Conclusion: In selected cases brachytherapy can be used as the last-line or palliative therapy for patients with advanced recurrence head and neck carcinomas. Possible complications and the reduction of quality of life due to tracheostomy should be considered.

Despite initially successful application of different combination therapies for squamous cell carcinomas of the head and neck, local recurrences cannot be avoided, with locoregional recurrence rates reaching approximately 15% to 50% (1-4). In these cases, patient care is ideally managed in a multidisciplinary setting. Various therapeutic modalities have been applied for the treatment of local recurrent disease, such as surgery, radiotherapy, and chemotherapy, alone or in combination. Especially for patients with prior radiation, cases of unresectable tumors, and cases complete surgical excision of the tumor where results in severe anatomic and functional defects, treatment options are limited. Interstitial brachytherapy can be used as a single measure or in combination with other treatment modalities. Interstitial high-dose rate brachytherapy (HDRB) allows for high-dose delivery into the tumor with sharp dose fall-off for the surrounding tissue. The efficacy of brachytherapy in unresectable advanced recurrence as a sole treatment modality has only rarely been studied in literature. The aim of the present study was to analyze patients who were solely treated with brachytherapy for unresectable, prior-irradiated, advanced recurrent squamous cell carcinoma of the head and neck.

Patients and Methods
A retrospective analysis of all patients who were treated with brachytherapy for advanced recurrence of squamous cell carcinoma of the head and neck was performed. Inclusion criteria for evaluation were that solely brachytherapy was performed for recurrent disease, no curative resection was possible and that the patients had previously undergone primary or adjuvant external-beam radiation. Medical records were reviewed regarding age at primary diagnosis and recurrence, TNM stage, previous treatments, dose and fraction of brachytherapy, complications and outcome.

All patients underwent brachytherapy needle implantation under general anesthesia (Figure 1). After preoperative computed tomography (CT) or magnetic resonance imaging (MRI) direct laryngopharyngoscopy and digital examination were performed to estimate the extent of the tumor. Hollow steel needles were inserted through the volume of interest from the skin to the mucosal surface (Figure 1A and 1C). Afterwards, plastic afterloading implants were inserted through the needles (Figure 1B). The needles were then removed, leaving the plastic catheters in place. Finally, the afterloading catheters were fixed with plastic buttons on the skin surface. After CT-based planning, brachytherapy with iridium-192 was performed. Removal of the afterloading catheters was performed one day after the last irradiation.
Results

Twelve male patients with histologically-proven advanced recurrent squamous cell carcinoma that had occurred in a previously irradiated area were considered unresectable but suitable for interstitial brachytherapy. At primary diagnosis the patients were 42 to 66 years old (average age=51.8 years) and staged as follows: Nine patients (75%) had Union Internationale Contre Cancer (UICC) stage IV, two (17%) stage III and one (8%) stage II disease. The initial treatment was surgery and adjuvant radio(chemo)therapy in seven cases and primary radiochemotherapy in five. The median interval between first treatment and brachytherapy was 8 years (range=12 months-15 years). The recurrences occurred in the base of the tongue in eight patients, in the floor of the mouth in three patients and in one patient in the tonsillar region. The ages of the patients at brachytherapy ranged from 52 to 73 years (average=59.8 years). Interstitial brachytherapy was performed with an iridium-192 source. Between 6 and 18 afterloading catheters were implanted under general anesthesia (Figures 1 and 2); in 10/12 patients, a tracheostomy was additionally performed. One patient had been tracheotomised before. Brachytherapy was administered with a mean tumor dose of 20-33 Gy, depending on previous radiation, in twice-daily fractions of 2-3 Gy per fraction. There were no serious complications; adverse effects were mucositis and edema. The afterloading catheters were removed one day after the last irradiation, in ten cases under general anesthesia.

The median survival of the patients after brachytherapy was 8.5 months (Figure 3). The shortest survival after brachytherapy was four weeks. A total of 10/12 patients died; eight at home, two in a hospice and one in hospital. No autopsies were performed. Out of these patients, five had a histologically-proven local recurrence after brachytherapy and four suffered from distant metastases.

The longest survival without local recurrence is now 4 years and 11 months. This patient has no evidence of local tumor recurrence. He has been treated for axillary metastases with surgery and adjuvant radiotherapy two years after brachytherapy and actually has axillary metastases again. This patient is still tracheotomised.

The second patient who is still alive was histologically-proven tumor-free. Therefore the tracheostomy was closed four months after brachytherapy. However, this patient now has a tumor recurrence 24 months after brachytherapy. After diagnosing the recurrence, the patient was re-tracheotomised and best supportive care has been initiated.

Discussion

Local failure is a common event and the most frequent cause of death of patients with head and neck cancer, despite completion of definitive treatment (5). Due to poor survival rates and potentially high associated morbidity, physicians must carefully weigh harm versus benefit when considering treatment options. The preference for resectable patients is
salvage surgery, with 5-year survival rates ranging from 16-36% (6-8). In many cases, salvage surgery is not feasible or often only possible with severe complications and limited success at the expense of functional and esthetic integrity. Whenever the morbidity of surgical resection outweighs its benefits, or the recurrent tumor is non-resectable radiation therapy is an alternative. Eighty percent of recurrences arise in previously high-dose irradiated volumes (9). In these cases, re-irradiation with external beam is often not possible because of the risk of toxicity, extreme morbidity and mortality. Moreover, radiation is impeded by less-defined anatomic locations after previous therapy.

Salvage brachytherapy for patients with recurrent disease after radiotherapy is a viable option. The indications for interstitial brachytherapy differ depending on the individual course of disease. Brachytherapy offers the possibility of concentrated, direct irradiation of the tumor with a high dose while sparing the surrounding tissue due to the rapid dose fall-off beyond the implant volume. There are some areas in the head and neck region which are especially suitable for brachytherapy, such as the mouth floor and the base of the tongue. These were also the most common locations in this study.

Successful treatment of tumors with interstitial brachytherapy requires high targeting accuracy of the brachytherapy needles to avoid harming vital anatomical structures, which can lead to severe bleeding. The surrounding structures at risk have to be taken into account. No fatal complications were seen in the presented patient group; late complications were not seen, perhaps due to the short overall survival of the patients. However, complications can never be excluded. Therefore the implantation of the needles and the application of brachytherapy should be carried out by experienced hands.

In literature, iridium-192 seed implantation as a sole modality showed promising results in the treatment of different malignant tumors. Several clinical studies of head and neck cancer patients have reported good local control results using brachytherapy, but only few studies had a similar setting to ours. Outcomes after re-irradiation of tumors are variable and 5-year survival rates range from 3.8% to 100% (10, 11).

In the present study, there was a poor overall survival. It should be borne in mind that in the presented cases, the disease was advanced, and especially after previous surgery, diffusely spread at the time of application of interstitial brachytherapy. Therefore, brachytherapy as last-line therapy is only suitable for a very selected group of patients with advanced recurrent head and neck cancer after previous full-dose radiation therapy.

Moreover, when a patient is diagnosed with recurrent disease, quality-of-life issues, such as postoperative complications, speech and swallowing function, become important concerns (12). In this study, ten patients had to be tracheotomized for brachytherapy due to bleeding risk and
swelling. One patient had already been tracheotomised before. Having a tracheostoma leads to a decrease of the quality of life, which has to be kept in mind, especially for patients with a poor prognosis.

The limitations of the current investigation include those inherent to its retrospective design. The sample size was limited to a group that underwent brachytherapy-alone for recurrent disease. Because of the small patient population, the conclusions that can be drawn are limited. However, the results of this investigation indicate that local control by brachytherapy is only possible in very selected patients with advanced recurrent non-resectable carcinomas of the head and neck. Aspects of treatment that are still not clearly defined include appropriate patient selection and the optimal dose of radiation that should be applied.

References


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