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Re-irradiation with interstitial pulsed-dose-rate brachytherapy for unresectable recurrent head and neck carcinoma

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ABSTRACT

PURPOSE: To assess the long-term results of protocol-based interstitial pulsed-dose-rate (PDR) brachytherapy combined with simultaneous chemotherapy in selected patients with recurrent head and neck tumors not amenable to salvage surgery.

METHODS AND MATERIALS: A total of 51 patients with recurrent head and neck cancer were treated with interstitial PDR brachytherapy. Forty patients (78%) had salvage brachytherapy alone using a median total dose of 60 Gy. Salvage brachytherapy in combination with external beam therapy was performed in 11 patients (22%) using a median total dose of $D_{REF} = 27$ Gy. Simultaneously with the PDR brachytherapy, a concomitant chemotherapy was administered in 35/51 (69%) of patients. The analysis was performed after a median followup of 58 months.

RESULTS: Local control rates calculated according to Kaplan–Meier after 2 and 5 years were 71% and 57%, respectively. Comparing results of salvage PDR brachytherapy with or without simultaneous chemotherapy, the 5-year local recurrence-free survival rates were 78.9% vs. 38.5% ($p = 0.01$), respectively. No other patient or treatment-related parameters had a significant influence on treatment results. A total of 9/51 (17.7%) and 6/51 (11.8%) patients developed soft-tissue necrosis or bone necrosis, respectively, but only 2% of patients required surgical treatment.

CONCLUSIONS: PDR interstitial brachytherapy with pulse doses between 0.4 and 0.7 Gy/h/24 h with simultaneous chemotherapy is an effective and safe option for curative therapy in selected patients with head and neck cancer in previously irradiated areas, which are not suitable for salvage surgery.

Keywords: Re-irradiation; Head and neck cancer; Interstitial brachytherapy; PDR brachytherapy; Salvage brachytherapy; Local recurrence

Introduction

Despite aggressive multimodality treatment protocols used in first-line treatment, a significant proportion of head and neck cancer patients develop locoregional recurrences typically during the first years of followup. Patients with recurrent head and neck cancer or a second primary tumor occurring in a previously irradiated area have generally a very poor prognosis. If surgery is not an option, the curative treatment possibilities are exceptionally limited (1, 2). Usually, the setting of re-irradiation is palliative and as a consequence the results of such treatments are very disappointing (3, 4). However, since 1990, it has been demonstrated through several studies that a multimodality approach of re-irradiation with simultaneous chemotherapy is feasible with long-term local control for a fraction of patients (5–14). The main advantage of interstitial brachytherapy is an extremely steep dose gradient between the prescription dose encompassing the tumor area and the surrounding healthy structures as the mandible, skin, healthy parts of the tongue or of floor of the mouth. These quality characteristics make it possible—at least theoretically—to provide excellent protection to these organs and structures to an extent and quality that would be unattainable using techniques of external beam radiation therapy. In addition to this fact, there are further properties of brachytherapy, which make this technique highly suitable for the purposes of re-irradiation—namely its high flexibility, high versatility, excellent precision, very good quality assurance,

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and reproducibility resulting from its lack of dependence on patient or organ motions. All these attributes of brachytherapy are excellent preconditions for good results of interstitial brachytherapy as a salvage treatment modality for recurrent head and neck tumors. Unfortunately, the majority of recurrent head and neck cancers are not appropriate candidates for brachytherapy alone because re-irradiation of local recurrences with brachytherapy is suitable only for small volume recurrent disease and for technically accessible locations of tumor recurrences.

A number of publications from the last decades (1, 5, 15−18) as well as our own first results (14, 19) have shown that interstitial salvage brachytherapy is feasible and could potentially be a curative option for these patients.

The aim of the present analysis was to assess the long-term results of protocol-based interstitial pulsed-dose-rate (PDR) brachytherapy combined preferably with simultaneous chemotherapy in a group of selected patients where salvage surgery was not possible.

Patients and methods

Patients

Between 1999 and September 2008, a total of 51 patients with biopsy proven, recurrent head and neck cancer not amenable to salvage surgery were treated with interstitial PDR brachytherapy in our department.

Criteria for eligibility for protocol-based salvage brachytherapy ± simultaneous chemotherapy and interstitial hyperthermia were as follows: histologically confirmed recurrent carcinoma of the head and neck region with no evidence of distant metastasis, tumor size and location suitable for brachytherapy techniques, good performance status, and radiation therapy completed more than 3 months ago. In patients with relevant comorbidities, which presented a contraindication to chemotherapy, we refrained from simultaneous chemotherapy. Likewise, for additional interstitial hyperthermia, we strictly selected patients with good compliance only.

Before diagnosis of the tumor recurrence, all patients had in the context of their previous antitumor treatment received radiation therapy up to a total dose between 60 and 76 Gy (median 65 Gy) with or without chemotherapy.

Re-irradiation

All patients were treated with interstitial PDR brachytherapy with or without external beam radiation therapy. The implant method was described by us in detail earlier (14, 20). The dose specification was done in all cases according to ICRU 58 (Paris system). A dose per pulse (dp) of 0.40 to 0.70 Gy (median 0.55 Gy) was given up to a median total dose of 57 Gy (range between 12 and 66.3 Gy). The pulses were delivered for 24 h per day, night and day, with a time interval of 1 h between two pulses.

Tumor response and toxicity

All patients underwent repeated examinations during and after therapy for evaluation of tumor response and side effects. Following the end of therapy, patients were followed at 3-month intervals for 24 months and thereafter at 6-month intervals for at least a further 60 months to analyze late side effects, local control, and survival. The side effects were scored according to the European Organisation for Research and Treatment of Cancer—Radiation Therapy Oncology Group Criteria and the Lent Soma criteria (21).

Statistical considerations

The primary end point of the analysis was to analyze local tumor control rate and late side effects at 5 years. Additional end points were disease-free and overall survival after 5 years. The median followup was calculated from the first day of re-irradiation to the date of last follow-up. Data management and statistics were carried out with PASW Statistics for MS Windows (SPSS Inc., Chicago, IL), release 21.0.0. For statistical comparisons between groups, the Mann−Whitney U test and Pearson's Chi-square test were used, as appropriate. Survival probability was estimated using the Kaplan−Meier method (22), using the log-rank test and Cox regression multivariate analysis to compare two or more groups.

Results

Patient population

The median followup of the patients was 58 months (24−76 months). The median time interval between the first and second radiation therapy, that is, retreatment with brachytherapy, was 27 months (range, 6−254 months).

Eleven of 51 (22%) patients were treated with second primaries and 40/51 (78%) with recurrent tumors. Detailed patient characteristics with regard to tumor site and tumor stage (Table 1) show that the majority of the patients had carcinoma of the tongue (61%) and ≥T2 tumors (90%).

Salvage brachytherapy

The median implant volume as measured by the volume of the reference isodose was 34.1 cm^3 (range, 7.2−77.1 cm^3). Further documented brachytherapy parameters included the V_{150}, the dose non-uniformity ratio, coverage index (V_{100}), and the D_{90}. Their median values were 7.6 cm^3, 0.25, 93.8%, and 99.2%, respectively.

Forty patients (78%) had salvage brachytherapy alone with a median total dose of 60 Gy. Salvage brachytherapy in combination with external beam therapy was performed in 11 patients (22%) with a median total dose of $D_{REF} = 27$ Gy. Here, the brachytherapy was administered