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Brachytherapy 12 (2013) 521–527

BRACHYTHERAPY

Interstitial pulsed-dose-rate brachytherapy for head and neck cancer—Single-institution long-term results of 385 patients

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ABSTRACT

PURPOSE: To assess the long-term results of protocol-based pulsed-dose-rate (PDR) interstitial brachytherapy (iBT) in 385 patients with head and neck cancer who underwent PDR-iBT preferably after minimal, nonmutilating surgery.

METHODS AND MATERIALS: From 1997 to 2009, a total of 385 patients received protocol-based PDR-iBT for head and neck cancer. Brachytherapy was preceded by surgery in most of our patients (326/385, 84.7%). Altogether, 246 of 385 patients (63.9%) received iBT alone and 135 of 385 patients (36.1%) in combination with external beam radiation therapy. The analysis was done after a median followup of 63 months.

RESULTS: The 5-, 10-, and 15-year local relapse-free survival rates according to Kaplan–Meier test for all analyzed patients were 85.8%, 83.1%, and 80.2%, respectively. The 5-, 10-, and 15-year overall survival and disease-free survival rates were 68.9%, 52.2%, and 44.1%, and 81.3%, 79.3%, and 76.3%, respectively. For N0-/N1- vs. N2-patients, we observed significantly different 5-year local recurrence-free survival rates with values of 92.3% and 73.7%, respectively ($p = 0.007$). No other patient or treatment-related parameters had a significant influence on treatment results. Serious late side effects, such as soft tissue or bone necrosis, were observed in 39 of 385 patients (10.2%) and 18 of 385 patients (4.9%), respectively.

CONCLUSIONS: The PDR-iBT with 0.4–0.7 Gy each hour, 24 h per day for patients with head and neck cancer is a proven, effective, and safe treatment method with excellent long-term data.
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Keywords: Pulsed-dose-rate brachytherapy; Interstitial brachytherapy; Head and neck

Introduction

Interstitial brachytherapy (iBT) as a sole treatment or in combination with external beam radiation therapy (EBRT) is a valuable treatment modality in the treatment of both primary and recurrent head and neck cancer. The results of low-dose-rate (LDR) brachytherapy with ^{192}Ir wires using the rules of the Paris system were considered gold standard in the therapy of preferably small head and neck tumors up to the end of 20th century (1–14). Pulsed-dose-rate (PDR) brachytherapy as a substitute for LDR brachytherapy is considered a useful option in the treatment of head and neck tumors because it combines the biologic advantages of LDR brachytherapy (15–18) with the technical advantages of the afterloading technique known from high-dose-rate (HDR) brachytherapy.

This article presents a single-institution experience of protocol-based PDR-iBT for 385 patients with special emphasis on local control rate and late toxicity in patients with squamous cell carcinoma of the oral cavity and of the oropharynx who underwent PDR-iBT preferably after minimal, nonmutilating surgery.

Patients and methods

From October 1997 to December 2009, 385 patients received protocol-based PDR-iBT for head and neck cancer. Patient and tumor characteristics especially with regard to tumor site and stage (Table 1) illustrate that most patients had tumors of the oral cavity (72%). Mainly, the

Received 23 April 2013; received in revised form 10 June 2013; accepted 3 July 2013.

Financial disclosure/conflict of interest: All authors do not report any financial disclosures or conflict of interest.

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http://dx.doi.org/10.1016/j.brachy.2013.07.002

Table 1
Tumor characteristics

Characteristics	Number of patients ($N = 385$), n (%)
Tumor site	
Lip	14 (3.6)
Floor of mouth	118 (30.6)
Base of tongue	33 (8.6)
Mobile tongue	160 (41.6)
Soft palate	12 (3.1)
Tonsil	34 (8.8)
Buccal mucosa	11 (2.9)
Nasopharynx	2 (0.5)
Hard palate	1 (0.3)
Tumor stage	
T1	172 (46.2)
T2	167 (44.9)
T3	17 (4.6)
T4	14 (3.8)
Tx	15 (4.0)
Nodal stage	
N0	253 (65.7)
N1	56 (14.5)
N2	57 (14.8)
Nx	6 (1.6)
Histology	
Squamous cell carcinoma	359 (96.5)
Adenoid cystic carcinoma	5 (1.3)
Others	8 (2.2)
Grading	
G1	38 (10.2)
G2	221 (59.6)
G3	101 (27.2)
G4	2 (0.5)
Not classified	2 (0.5)
Not known	21 (5.4)
Lymphovascular invasion	
Negative	197 (53.1)
Positive	87 (23.5)
Not known	101 (27.1)

tumors (70%) were well or moderately differentiated squamous cell carcinomas with 91% being in Stage T1/T2.

In most of our patients (326/385, 84.7%), brachytherapy was preceded by surgery. The surgical procedures for all these patients included tumor resection with neck dissection. The time interval between surgery and radiation therapy was 63 days (median). The indication for postoperative brachytherapy predominantly was positive or close resection margins (≤2 mm), or in the case of clear resection margins if there were risk factors such as a depth of tumor invasion of more than 5 mm, lymphovascular invasion, or histopathologic grading of 3 or 4. Clear resection margins had been achieved in 300 of 326 (92%) patients. The median value for depth of tumor invasion was 7.0 mm. A total of 139 of 385 patients (37.4%) with large tumors or positive lymph nodes were treated in addition with EBRT with a median dose of 55 Gy. The median for the time interval between EBRT and brachytherapy was 9 days. All patients were treated with PDR-iBT with ^{192}Ir. All implants were done under general anesthesia using plastic tubes and respecting the rules of International Commission on Radiation Units and Measurements 58 (19) as described by us in detail earlier (20, 21). A dose per pulse (dp) with a median value of 0.55 Gy (range, 0.4–0.7 Gy) was used, delivered for 24 h per day with a time interval of 1 h between pulses. The median volume of the 85% isodose (reference isodose) was 23.4 cm^3. The median values for the dose homogeneity index and the dose nonuniformity ratio were 0.76 and 0.27, respectively. For 113 of the 385 (29%) patients treated since 2007, a delineation of the clinical target volume (CTV) and the organs at risk using CT-based treatment planning has also been performed. The CTV encompassed the macroscopic tumor/tumor bed (gross tumor volume) and a 5–10-mm safety margin in all directions respective of natural, anatomic borders such as bone, the lingual edge, and the skin. In postoperative cases, the tumor bed contour (gross tumor volume) included all clinically visible and palpable surgical scars. For CT-based planning, the dose distribution was normalized on reference points in the central plane according to International Commission on Radiation Units and Measurements 58. Thereafter, a geometric optimization was done to achieve the best possible dose homogeneity. In a last step, the dwell times were adjusted manually or using graphical optimization aiming to achieve a satisfactory coverage of the CTV. Here also, the coverage index V_{100} (median, 93.3%) and D_{90} (median, 103.8%) were documented.

A total of 246 of the 385 patients (63.9%) received iBT procedures alone using a median total dose of 57 Gy. In combination with EBRT, PDR-iBT was performed with a median total dose of 24 Gy. The median time interval between external irradiation and brachytherapy was 9 days. The EBRT was performed up to a median reference dose of 55 Gy.

Patients with T4 tumors or positive lymph nodes with extracapsular tumor extension (47/385, 12.6%) additionally received simultaneous chemotherapy in the first and fifth weeks of EBRT using Cis-/Carboplatin and 5-fluorouracil.

The statistical analysis was performed with the SPSS 18.0 software (IBM Corp., New York). The actuarial curves were calculated according to the Kaplan–Meier method (22). The comparisons were made using the log-rank test or Cox regression analysis or the Kruskal–Wallis test as appropriate. All patients were followed closely to analyze local control, survival, as well as acute and late toxicity. The analysis was performed after a median followup of 63 months. The followup was calculated from the first day of radiation therapy to the date of last followup.

Results

The 5-, 10-, and 15-year local relapse-free survival rates according to Kaplan–Meier test for all analyzed patients were 85.8%, 83.1%, and 80.2%, respectively (Fig. 1). The 5-, 10-, and 15-year overall survival and disease-free

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